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PAPILLOMATOUS DISEASE OF THE RENAL PELVIS*

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THE study of this disease has suffered greatly because, owing to the rarity of these tumours, only isolated instances are published and because the report appears shortly after the discharge of the patient from hospital and before the results of treatment can be assessed. No further report tells of the patient's ultimate fate. There is an extensive literature of this type and comparatively few papers in which a list of cases followed over a sufficient period appears.

The present paper reviews 19 examples of this disease collected over a period of 29 years and the patients have been carefully followed, making it possible to take a long-term view and to judge the remote results with some accuracy. These do not always bear out early expectations. One can scarcely fail to be struck with the great diversity amongst these specimens,† not only as regards the size and position of the tumours but also on account of the variety of their effects on the proximal and distal sections of the urinary tract.

Little was known about the disease before the commencement of the present century. At that time Albarran (1903) was able to find only 42 examples in the literature. Various compilations of cases have been made since then, each adding a few examples to a preceding list. The most important is that of Swift Joly (1933) who made an exhaustive hunt, including a widespread questionnaire, and discovered 337 pelvic tumours, of which 126 were hitherto unpublished. Further cases have been published since that time. The proportion which pelvic growths bear to growths of the kidney in general has been estimated by a number of writers, but Kutzman (1938), collecting and analysing these, computed that prior to 1920 the pelvic tumours constituted 5·2 per cent of all renal neoplasms and that from that date till 1937 the figure rose to 6·4 per cent.

CASE REPORTS

Case 1.—A. B., male, aged 45. *Papilloma of the renal pelvis.*

"Symptomless hæmaturia", traced to the right kidney, which was enlarged on palpation.

Specimen (*Fig.* 110) shows a papilloma about the size of an egg, with well-formed villi. There are numerous secondary splashes on those parts of the pelvis which are not primarily affected. The growth is luxuriant in type and a similar growth in the bladder seen cystoscopically would be diagnosed as benign. The papilloma appears to fill the pelvis completely, and one would have expected it to become impacted in the renal outlet, but there was no hydronephrosis.

This was an early case (1917) and the importance of removing the ureter was overlooked. For several days after operation blood in quantity was observed in the urine and the question of bleeding from ureteric implants inevitably arose. Blood must have arisen from operative trauma, for it disappeared and the patient was well at the end of eight years.

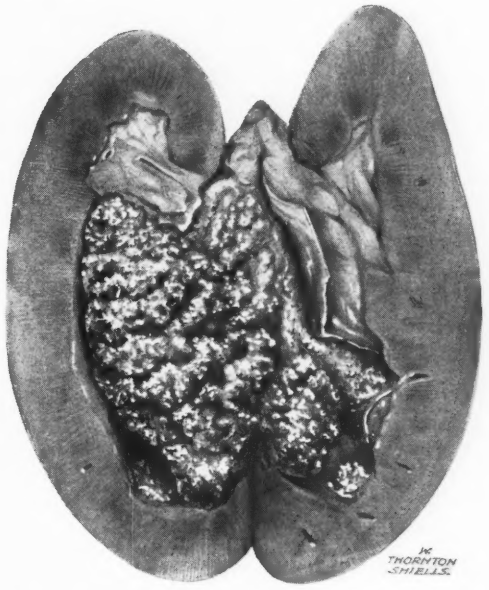

FIG. 110.—*Case* 1. Benign papilloma of renal pelvis. Luxuriant type. Secondary splashes. Singular absence of pyelectasis.

Comment.—This specimen is interesting as showing papillomatous disease in its simplest, most uncomplicated form. It was my first specimen and remains unique in the way it exhibits a benign growth together with its local satellites. In view of the number of these satellites further growths in the ureter might have been anticipated, but the subsequent satisfactory history excludes them. The habit of forming superficial implants is common enough in the bladder, but is even more pronounced with the villous-covered tumours of the pelvis and ureter. It has been said that the most characteristic feature of papillomata of the renal pelvis is the tendency to sprout and propagate within the urinary tract. A

* Hunterian Lecture delivered at the Royal College of Surgeons on Jan. 9, 1947.

† With two exceptions all the specimens were displayed in the body of the hall and are now in the College Museum.

number of the cases which I shall demonstrate support this statement and show its importance in the evolution and handling of the disease. It might have been expected that this villous tumour would at some time have plugged the renal outlet with a frond, but there was no symptomatic evidence of this and no hydronephrosis. At operation the tumour was felt as a doughy mass within the pelvis and the same observation has been made on two other kidneys (*Cases* 6, 7). It is a useful sign. The sensation is as of something resembling a plug of wet cotton-wool in the pelvic cavity and nothing else I know gives quite the same feeling. In all three cases the walls of the pelvis lay loosely over the tumour and could be pinched up with the fingers from any area to which the tumour was not actually attached.

Case 2.—Mrs. A. T., aged 60. *Carcinoma of transitional epithelium.*

March 6, 1941: Admitted as emergency with severe hæmaturia. Blanched.

Hæmaturia: First attack nine years previously. For three months constant and profuse. Bright red blood.

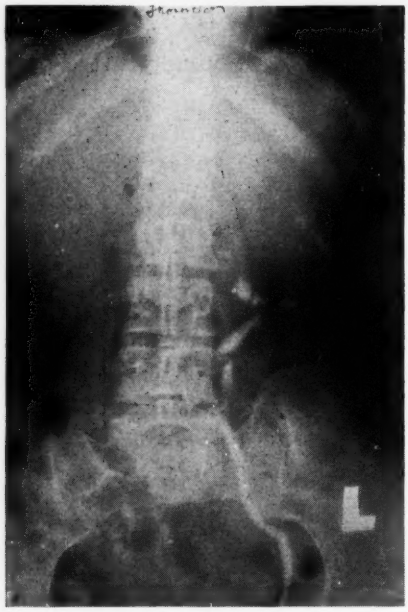

FIG. 111.—*Case* 2. Retrograde pyelogram. Obstruction of ureteropelvic junction is well shown. Pyelectasis not demonstrated. Kidney lies low. Tortuous ureter.

Pain: Burning pain across lower back.

Micturition: No difficulty. No frequency.

Loss of weight: Marked.

ON EXAMINATION.—Right kidney easily palpable but not much enlarged. P.V., nil. Bladder not palpable. Pallor and weakness pronounced.

Urine bright red.

Blood-count: Blood group II. Hæmoglobin 34 per cent. Mean diameter 6·9 cm. Red cells 2,200,000/c.mm. Colour index 0·8. W.B.C.'s 5000/c.mm.

Blood-film: Leucocytes nil to note. Reds show anisocytosis. Occasional poikilocytosis. Many were hypochromic.

Cystoscopy (March 8): Urine withdrawn bright red. Washed clear easily. Bladder mucosa very pale, shows no other abnormality. L.U.O., profuse hæmorrhage; R.U.O., injected but no hæmorrhage. Indigocarmine: R.U.O., 3½ minutes, good; L.U.O., nil after 8 minutes.

Retrograde pyelogram (left) (*Fig.* 111): Kidney displaced downwards, the ureteropelvic junction lying opposite the fourth lumbar vertebra. Very little fluid entered the pelvis, and that only the lowest portion. The ureter is tortuous. Two calcified shadows seen in renal area.

March 12: Transfused.

FIRST OPERATION (March 13).—Spinal anæsthetic. Right lumbar nephrectomy with about 4 in. of ureter. Operation smooth.

THE SPECIMEN (*Fig.* 112).—Two large papillomata of renal pelvis, one occupying the ureteropelvic junction, the other extending into the lower calices. Pronounced

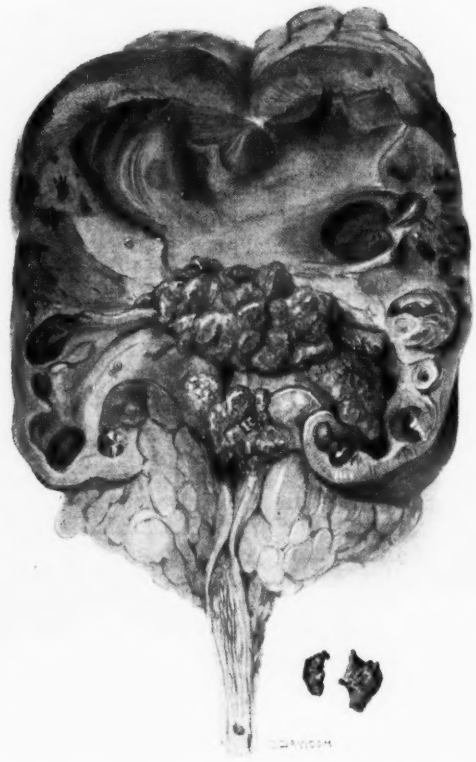

FIG. 112.—*Case* 2. Two papillomata of pelvis, one blocking outlet. Hydronephrosis. Note small cystic lesions in upper and lower calices and in ureter.

dilatation of upper calices. Several small cystic lesions seen in the upper and lower calices and in the ureter. Two small irregularly spiculated stones.

Pathological Report.—Carcinoma of transitional epithelium.

SECOND OPERATION (April 18).—Ureterectomy completed. Superficial ulceration of the mucosa. No neoplasm.

Convalescence smooth. Good recovery.

July, 1945: Reported well.

Comment.—In this and the succeeding case the long history, together with the pathological report of malignancy, seem to indicate a recent metaplasia. In each note the blocked outlet and its effect on the pyelogram and compare *Case* 5 and *Case* 15.

Case 3.—Mrs. M. H. F., aged 69. *Carcinoma of transitional epithelium.* (Referred by Dr. Sankar, Heywood.)

First seen on March 31, 1944.

Hæmaturia: Onset 12 years ago. Intervals have often been 12 to 18 months and then the attacks have been mild. Recently (3 weeks) severe, continuous, and clots marked.

Pain in left side: If pain is present, no clots; if pain disappears, clots passed.

On Examination.—Large mass in left loin, the size of fœtal head. Mobile, firm. Very pale. Has lost much weight.

Previous medical history: Both breasts removed, 14 and 26 years ago. Incisions go to axillæ. Pectoralis major absent.

Urine: Blood marked, clots numerous.

Cystoscopy (July 9): Urine clear. Capacity normal. A spherical solid neoplasm is present at the L.U.O., the size of a walnut. Impossible to see or catheterize L.U.O. Indigo-carmine: R.U.O., 4½ minutes, good; L.U.O., none after 8 minutes.

Excretion urogram: The left kidney is not functioning. Right normal. Cystogram shows no filling defect.

Blood-count (July 13).—Hb 68 per cent. R.B.C.'s 4,190,000. C.I. 0·82. W.B.C.'s 7200. Blood-urea 40 mg. per cent. Blood group, II.

Transfusion of 1 pint of Group II blood was commenced about 10 p.m., but discontinued after ½ pint had been given about 12.15 a.m. because of a mild reaction.

Operation (July 14).—Spinal anæsthetic. Nephrectomy and partial ureterectomy. Large kidney delivered into wound. During this procedure peritoneum was opened in two places and sutured. Kidney was not adherent to surrounding structures, but there were hard enlarged lymph-glands around renal pedicle and in para-aortic region. The ureter was clipped and divided by diathermy knife and ligatured below pelvic brim. A mole of about 1¼ in. diameter was excised during the making of the skin incision. Histology, benign.

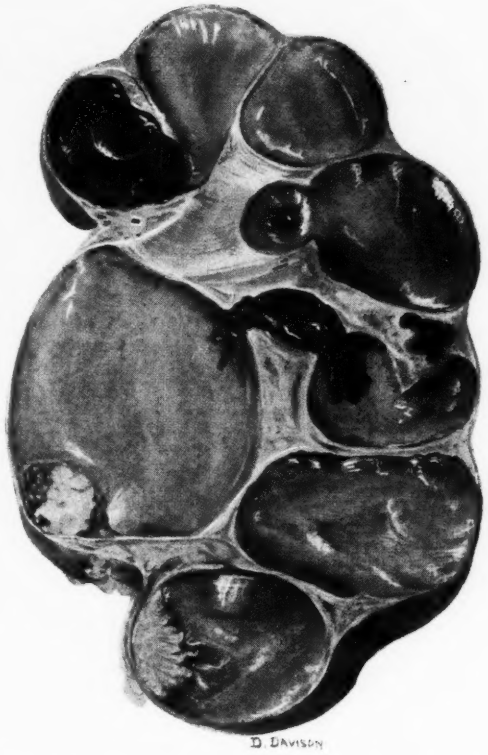

Fig. 113.—*Case* 3. Papillo-carcinoma of renal outlet. Distension of kidney with greenish colloid material. Long history (*see text*).

The Specimen (*Fig.* 113).—A hydronephrotic kidney with a smooth, but irregular, exterior. There was a hard mass at the ureteropelvic junction. Pelvis greatly dilated. The renal parenchyma, except for a few columns of Bertini, was atrophied and the space was occupied by a jelly-like, greenish, pigmented material. Ureter not dilated nor thickened.

Pathological report: Carcinoma of transitional epithelium.

Aug. 10: Discharged to own doctor. Progress satisfactory. In view of the inoperable glandular involvement the vesical growth was not proceeded with. This patient has not been traced, but the prognosis was very unfavourable.

Comment.—*See* note on preceding case. Also note the gross and long-standing hydronephrosis and the jelly-like nature of the contents. Growth in glands was seen at operation, which is not very common in this disease.

Case 4.—Mrs. C., aged 52. *Papillo-carcinoma of renal pelvis* (*left*). *Hæmatonephrosis. Stone.*

Admitted Nov. 14, 1930, as an emergency because of extreme exsanguination. Blood transfusion on admission.

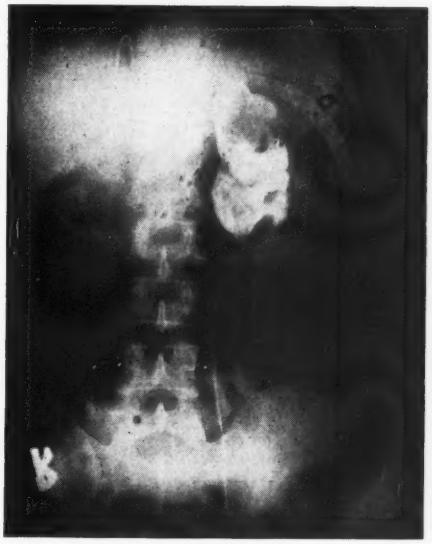

Fig. 114.—*Case* 4. Retrograde pyelogram. Large pelvis with filling defects caused by (*a*) blood-clot, (*b*) stone. Not by the small growth.

Bleeding only present four weeks; very severe for ten days.

Radiograph shows laminated stone at ureteropelvic junction.

Cystoscopy (Nov. 18, 1930): Mucosa normal but strikingly pale. Continuous thick tarry stream from the left ureter which mixed but slowly with the bladder contents.

Indigo-carmine: R.U.O., 4½ min. good efflux; L.U.O., no blue in 10 min. Pyelography (*Fig.* 114) shows dilatation of pelvis to the size of a small orange. No sign of calices remains. Stone shadow identified and obviously blocking renal outlet. Filling defects probably due to clots.

Operation.—Nephrectomy. The specimen (*Fig.* 115) shows a thin-walled sac with no renal substance discernible, the parenchyma being converted into a thin fibro-fatty wall. The contents are blood-clot and urine. Outlet blocked by stone with inorganic nucleus and thickly covered by laminated blood-clot (*Fig.* 116). A small sessile papilloma, ¾ in. in diameter, is found to occupy a position which suggests origin from the region of the calices. The removal of the remainder of the ureter took place two months later. It was apparently healthy.

Comment.—A continuous thick tarry stream of altered blood emerging from the ureter is apparently

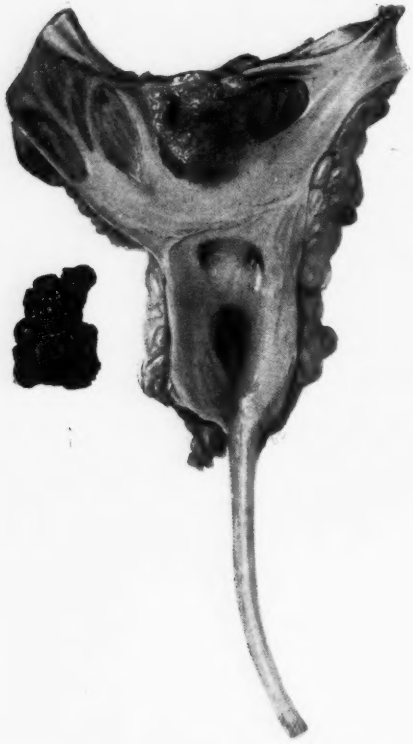

FIG. 115.—*Case* 4. Papillo-carcinoma of pelvis. Stone impacted in outlet. Advanced renal atrophy. Growth is away from renal outlet.

characteristic and has been remarked upon by Thomson-Walker and others. It is legitimate to assume that the stone was the primary factor in this case and led to the

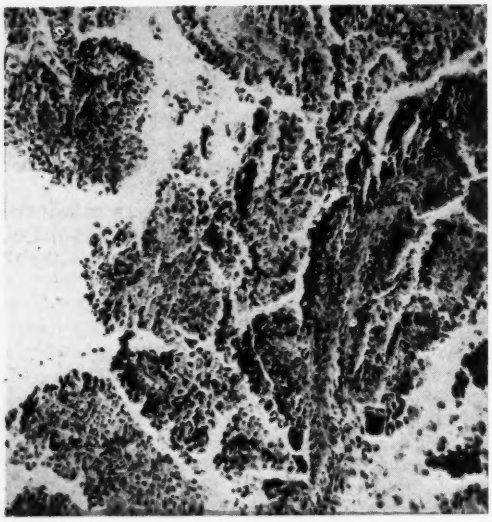

FIG. 117.—*Case* 4. Microscopical section. Papillo-carcinoma, active, irregular structure.

dilatation of the pelvis and destruction of the kidney. The papilloma is a small one and its microscopical appearances (*Fig.* 117) show that it is of an active type and therefore a recent comer. An examination for leucoplakia of the pelvic mucosa was negative. The patient died two years later with secondaries locally and

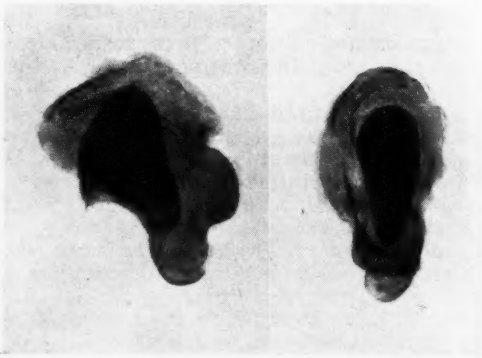

FIG. 116.—*Case* 4. Stone. Radiograph taken after removal shows a primary stone surrounded by layer of blood-clot.

in liver, etc. The papilloma is too small to produce a filling defect in the dilated pelvis. The mottled appearance of the pelvis is due to blood-clots.

Case 5.—Mr. J. W., aged 63. (Seen with Dr. Tingley, Pendleton).

Jan. 28, 1936: Commenced with hæmaturia, painless. For two days bright red, then smoky. No other symptoms. General health excellent.

P.M.H. and P.S.H., good.

Excretion urography: Right kidney normal, left no excretion.

Cystoscopy: Healthy bladder. Indigo-carmine: R.U.O., 3½ min., good; L.U.O., nil.

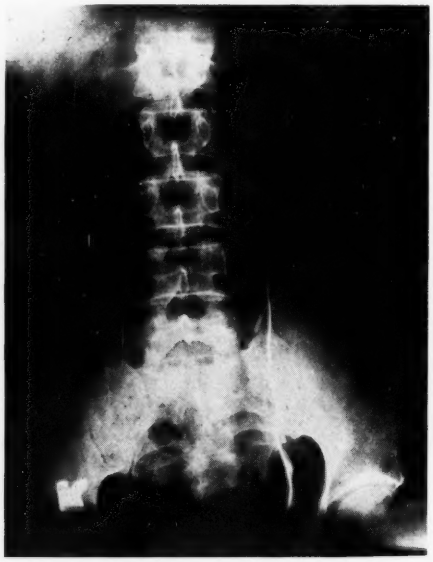

FIG. 118.—*Case* 5. Retrograde pyelogram. Catheter is forbidden entrance to the pelvis and but little fluid penetrates, failing to give a picture of the extent of the distension.

Retrograde pyelogram (*Fig.* 118): Catheter would not enter the renal pelvis and the only pelvic shadow displayed after injection was that of a small irregular area close to the ureteropelvic junction.

March 6: Nephrectomy (*Fig.* 119). Ureter not removed. Subsequent ureterectomy recommended but refused.

Pathological Report (*Fig.* 120).—Big central villus with well-formed branching villi. Fairly good pattern but some vacuolation. Benign.

Sept. 15, 1938: Very well. "Never a day's illness." No hæmaturia. No frequency. Urine clear. Wound excellent. Weight increased 18 lb. since operation.

FIG. 119.—*Case* 5. Area of pelvic outlet occupied by multiple papillomata. Hydronephrosis.

Comment.—The pyelogram shows blocking at the the ureteropelvic junction with obstruction to catheter and pyelographic fluid. Ureterectomy refused, but patient remains well.

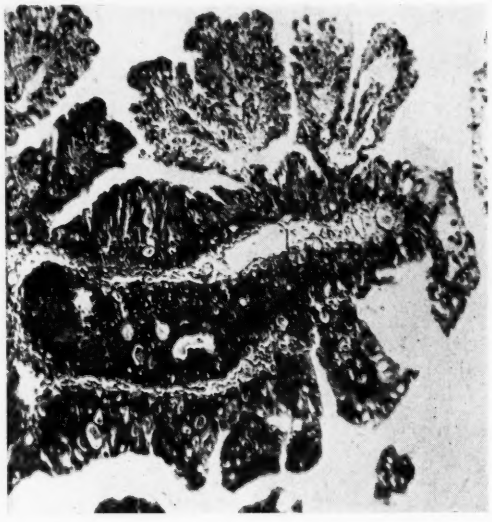

FIG. 120.—*Case* 5. Microscopical section. Moderately good pattern, vacuolation.

Case 6.—Jas. K., aged 69. *Benign papilloma of the renal pelvis.* (Referred by Dr. Gray, Tyldesley.)

July 12, 1943: Hæmaturia. Short duration. Slight. Repeated three months later.

Cystoscopy: Normal bladder. Indigo test: Both sides satisfactory in 5 min.

Excretion urogram: Both kidneys excrete the dye slightly subnormally. The pyelographic appearances are normal. Cystogram normal. Urine healthy in intervals. Source of blood at present untraced. Told to report when bleeding.

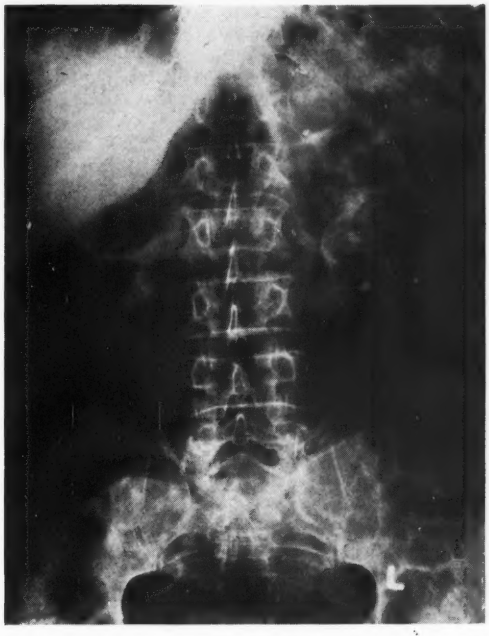

FIG. 121.—*Case* 6. Intravenous pyelogram shows filling defect accurately delineating the larger papilloma.

Dec. 9: Urine very hæmorrhagic.

Cystoscopy: Blood-stained efflux from L.U.O.

Descending pyelogram (*Fig.* 121): Filling defect size of a damson centrally placed in the pelvis. No pyelectasis. (Cf. *Fig.* 122.)

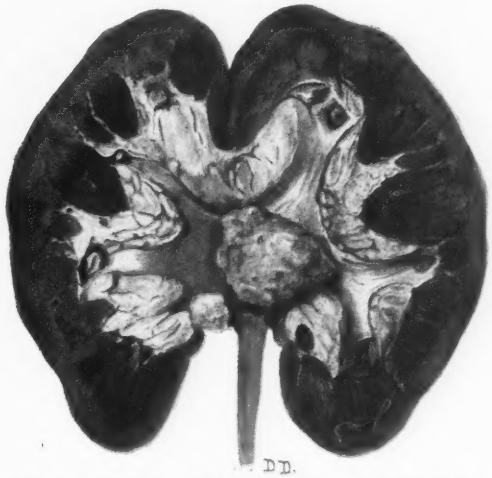

FIG. 122.—*Case* 6. Benign papilloma, size of a damson, a second the size of a pea. No pyelectasis.

Opinion: A well-defined, rounded defect like this is not likely to be due to a blood-clot. Probably a pelvic tumour.

OPERATION.—Nephrectomy with ureter to the pelvic brim. The ureter in this section was healthy and in view of the patient's age a second operation was not advised, the more so as the tumour was benign, small, and the symptoms recent. Note also the fine line of the ureter

seen on the urogram which suggests absence of obstruction. At operation the soft pulpy tumour could be quite definitely felt through the pelvic wall, thus confirming the diagnosis.

THE SPECIMEN (*Fig.* 122).—Shows a papilloma the size of a damson accurately accounting for the filling defect and a second small one nearby.

April 27, 1946: Patient in excellent health.

Comment.—(1) Initial difficulty in diagnosis. (2) Rounded filling defect subsequently displayed is typical and accurately delineates the lesion. (3) Doughy body felt at operation in the pelvis. (4) No ureterectomy (age 69), but well three years later.

Case 7.—Mrs. F. A. H., aged 61. (Referred by Dr. Howard English.)

HISTORY.—Hæmaturia: (1) September, 1944, lasted fifteen days; (2) Christmas, 1944, lasted one week; (3) May 19, 1945, lasted till first seen, May 22.

No other symptoms.

Previous medical history: Gall-stones and large duodenal diverticulum proximal to the duodenojejunal flexure and extending down to the right iliac fossa, giving rise to symptoms resembling angina. Operated on by Professor J. Morley eleven years previously.

ON EXAMINATION.—Urine healthy. External examination negative.

Radiograph negative, except for osteo-arthritis of the spine.

Excretion urogram, filling defect of the upper calix.

Cystoscopy: Urine a little hazy. Bladder healthy.

Indigo-carmine: L.U.O., copious in 3 min; R.U.O., at 4½ min., not so copious.

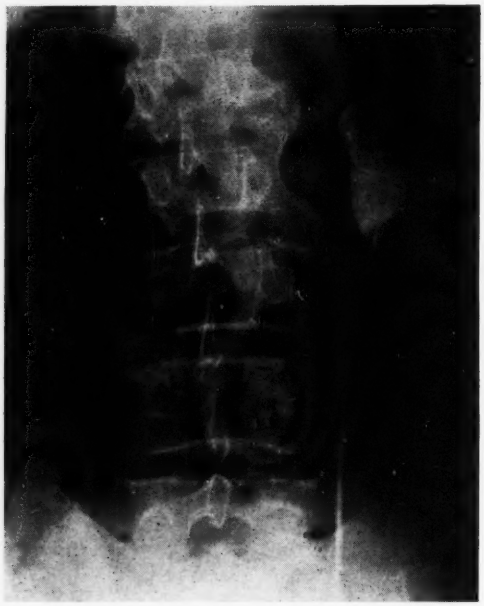

FIG. 123.—*Case* 7. Retrograde pyelogram. Pronounced filling defect and distension of upper calicine area. Other calices normal.

Retrograde pyelogram (*Fig.* 123): Considerable enlargement and deformity of upper calix, with pronounced filling defect strongly suggesting a growth, probably primarily pelvic. Middle and lower calices faintly shown but are normal.

OPERATION (May 23).—Nephro-ureterectomy. Kidney lay low. A soft lump could be felt in the pelvis and over it the pelvic wall could be moved.

THE SPECIMEN (*Fig.* 124).—Shows a soft, mushy growth of the upper calix extending into the pelvis proper. The walls of the calix are extensively eroded with papillomatous tissue over a wide area. No growth observed in the ureter.

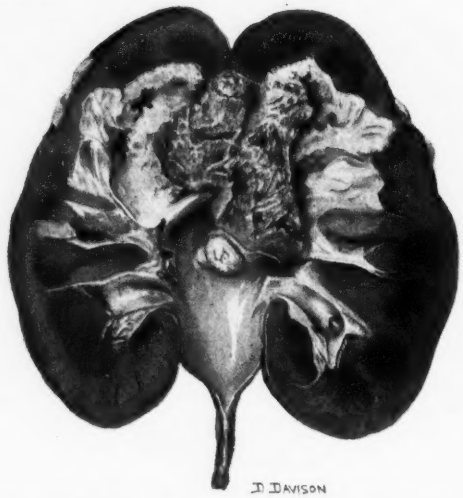

FIG. 124.—*Case* 7. Large papilliferous growth of upper calix. Cf. pyelogram, which gives a strikingly accurate impression.

Microscopical Report.—Two sections: Both show a papilloma of transitional epithelium. The base is fairly well defined and the nuclei are not abnormally active.

PROGRESS.—Uneventful.

Oct. 7, 1946: Patient very well.

Comment.—Examination of the pyelogram side by side with the drawing of the kidney shows how closely the former portrays the latter.

Case 8.—Male, aged 56.

Hæmaturia only symptom. Cystoscopy and X-ray examination negative. Hæmorrhage traced to left ureteric orifice. Indigo-carmine delayed.

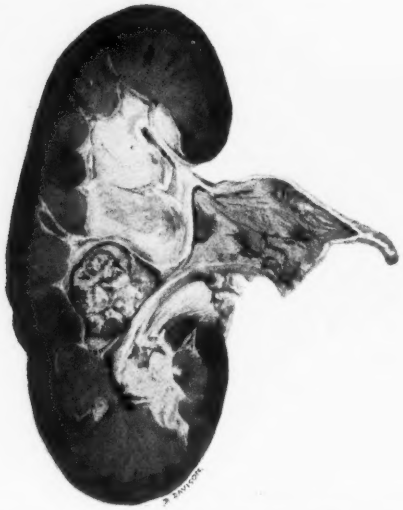

FIG. 125.—*Case* 8. Papilloma in calix with daughter growths in pelvis.

The specimen shows a papilloma the size of a marble, occupying the position of the lower renal calix. Many small tumours are distributed over the mucosa of the pelvis, mostly not larger than a millet seed. The growth in the calix appears to be the primary one, the others being satellites. No hydronephrosis. (*Figs.* 125, 126.) Professor Dean (then at the Manchester University)

regarded the calicine growth as primary, and of the secondaries in the pelvis some were reported encephaloid in type and some scirrhous.

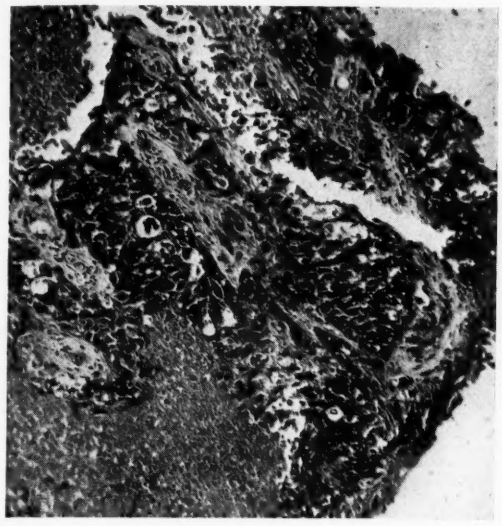

FIG. 126.—*Case* 8. Micrograph of primary tumour. (× 80.)

The case is interesting as showing a primary growth situated in a calix with secondaries from it occurring in the renal pelvis. Ureterectomy performed at a later date.

Comment.—This specimen is interesting as presenting separate growths of encephaloid and scirrhous types and because of the origin in a calix. Amongst the cases presented there are three growths in this identical position. The other two cases follow on this one.

Case 9.—S. P. L., female, aged 49.

First seen May, 1929. Symptomless hæmaturia, intermittent, four months. Never severe. Slight right-sided clot colic on one occasion. Examination negative, very stout. Urine examination and X-ray negative.

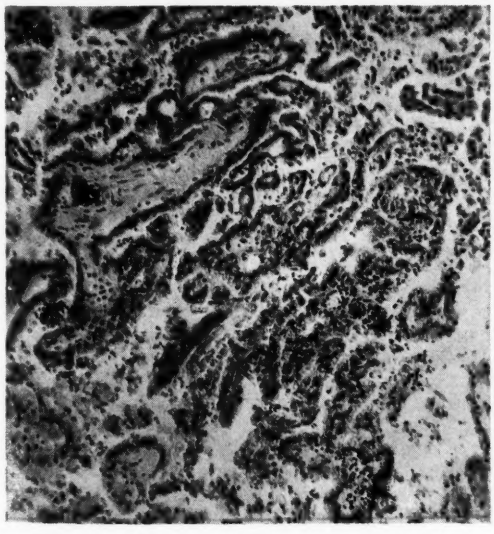

FIG. 127.—*Case* 9. Microphotograph of papillo-carcinoma.

Cystoscopy (May, 1929): Bladder healthy. Indigo-carmine: Right, 6 min., good efflux; left, 3¼ min., strong efflux. Diagnosis not made. June 6: During a period of bleeding blood seen coming from R.U.O.

Right retrograde pyelogram: Deformity of lower middle calix suspected.

OPERATION (June 27).—Nephrectomy followed by ureterectomy ten days later.

THE SPECIMEN.—Papilloma occupying a lower calix. No daughter papilloma observed. No papilloma in the ureter.

Pathological Report (*Fig.* 127).—Some of the fronds show the appearances of a simple papilloma, but one or two foci show definite malignant features with clusters of atypical cells, some of which are vacuolated and some unduly mitotic.

PROGRESS.—Recovery uneventful. Only cystoscopy permitted at the end of a year. Healthy bladder.

AUGUST, 1946: Remains well.

Case 10.—*Kidney showing papilloma of the pelvis*, removed from a girl aged 12 years by Mr. R. L. Newell, April 19, 1926.

M. T., aged 12 years, was admitted to the Manchester Northern Hospital on Nov. 11, 1925, with the history of having had intermittent attacks of severe hæmaturia since the age of 9. She had received treatment at another hospital but no diagnosis had been made.

On examination there was nothing abnormal to be detected. Both X-ray and cystoscopic examinations were negative. She remained in hospital fourteen days, but there was no further hæmaturia.

She was allowed to go home with instructions to her parents to bring her back immediately there was another attack. This they did three times, but each time the hæmorrhage had ceased. It was on the fourth occasion, on April 14, 1926, that a cystoscopic examination revealed blood spurting freely from the right ureter.

On April 19 the right kidney was removed. She made an uninterrupted recovery and is at the present time (1947) well and free from symptoms.

Comment.—The age of this patient is noteworthy—she was only 9 years of age at the time of her first bleeding. Swift Joly traced only two patients before the age of 10. Thomas and Regnier mention a squamous-cell carcinoma in a child of 3½ years and McDonald and Priestley a patient who " was less than 10 years of age ".

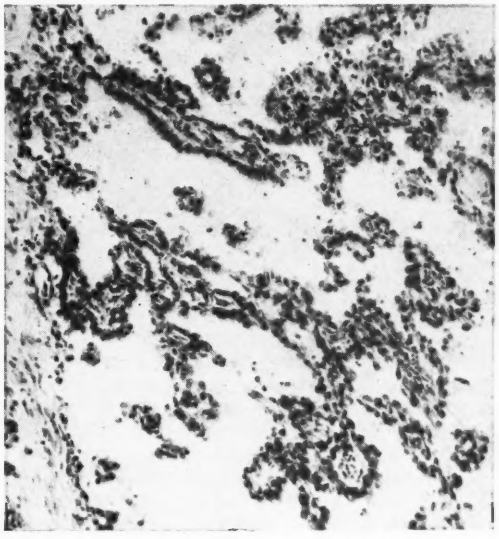

FIG. 128.—*Case* 11. Papillomatous material removed from supraclavicular gland (*see text*).

Case 11.—Mr. A. B., aged 38. (Seen in consultation with Dr. H. Cooper.)

Slight epididymitis three weeks previously of unknown origin. No pyuria. Recent hunting accident to back.

One week after epididymitis left colic and hæmaturia. Characteristic worm-shaped clot passed.

Investigation arranged but delayed because of business engagements.

In the interval developed hæmoptysis and pleurisy —seen by Dr. Kletz. Apparently settled down completely.

Arrangements again made for investigation but a left femoral thrombosis caused further delay.

Also developed abdominal pain and pain in the left loin of uncertain origin.

During recovery from this developed a gland above the inner end of the left clavicle. This softened and was excised. Section showed papillomatous tissue of the type found in the urinary tract (*Fig.* 128).

Patient's health deteriorated fairly rapidly. He developed intestinal obstruction four months after the original onset and died in 36 hours.

Comment.—This was evidently a papillo-carcinoma of the left kidney with severe metastasis, possibly precipitated by a hunting accident. Amongst Swift Joly's cases is one in which a patient developed a gland in the left supraclavicular fossa. The patient was a boy of 13 who had an apparently benign papilloma of the middle calix. "Four years later enlarged glands were found in the left supraclavicular fossa, one of which was excised and proved to be secondary to the kidney tumour. Six months afterwards he died of generalized carcinoma."

Cases with Secondary Growths in the Ureter

The succeeding 6 cases illustrate the development of ureteric growths secondary to those of the renal pelvis. The first 3 cases were nephrectomized prior to coming under the author's care for the treatment of their ureteric secondaries. Four of these 6 patients had also a vesical implant.

Case 12.—Male, aged 49. *Papilloma of the ureter secondary to renal papillomata.*

History.—Summer, 1926, slight hæmaturia. May, 1927, right nephrectomy by another surgeon. June, 1928, occasional hæmaturia. July, 1928, suprapubic operation for vesical papillomata. February, 1929, fresh hæmaturia treated by another suprapubic operation-diathermy. At this time there was a 'lighting up' in the neighbourhood of the renal scar. Aspirated twice and blood-stained fluid evacuated; also "the swelling voluntarily burst and a fair quantity of blood was emitted". June, 1929, severe but markedly intermittent hæmaturia.

The patient volunteered the statement that his urine was liable to be heavily stained on one passing and perfectly clear on the next, discomfort in the side being occasionally present during a blood-free period.

Sept. 15, 1929: First seen by me. Bladder found to be slightly infected but free from papillomata.

Sept. 21: Total ureterectomy.

The Specimen (*Fig.* 129).—Shows a carpet of papillomata in the lower two-thirds of the ureter, increasing in thickness towards the lower end.

Subsequent cystoscopies showed no further papillomatous disease in the bladder. In the spring of 1932 a lump re-formed at the site of the renal scar. Hæmorrhagic fluid was evacuated and tissue from the wall showed papillomatous material (*Fig.* 130). Under irradiation the swelling disappeared, but again showed itself in the summer of 1934 and proved resistant to treatment. Secondaries in the spine, with erosion of the lumbar vertebra (2nd), became evident in December, 1934. Transverse myelitis.

The patient died in 1936, i.e., ten years after onset of symptoms and nine years after nephrectomy.

Comment.—This case and specimen illustrate admirably many important features of this disease:—

1. The results of spilling papillomatous tissue into the wound—recurrence in and breaking down of the scar with eventual invasion of the body of a lumbar vertebra.

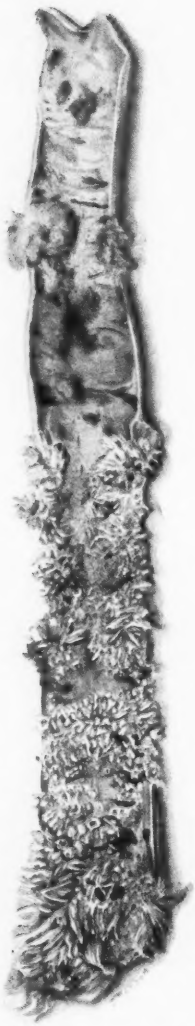

Fig. 129.—*Case* 12. Ureter removed two years and four months after nephrectomy for papillomatous disease. Note: (1) Multiplicity of growths; (2) Shortness of villi; (3) Accumulation at lower end of ureter; (4) Dilatation of ureter.

2. The impossibility of dividing the ureter without going across papillomatous tissue.

3. The low carpet of papillomatous growth which is so characteristic, and the multiplicity of the growths, far in excess of what is customary in the bladder.

4. The site of election is the lower part of the ureter, possibly because exfoliated cells, potential grafts, are temporarily held up here under compression and are perhaps squeezed against the ureteric wall.

5. The dilatation of the tube to accommodate the new growths.

6. Multiple bladder recurrences and failure to recognize their true cause.

7. The temporary improvement of the scar recurrences under deep X-ray therapy.

8. The long period which may elapse before death ensues (ten years in this case).

When subsequent cases repeat some of the above features it will be considered unnecessary to draw the reader's attention to them again.

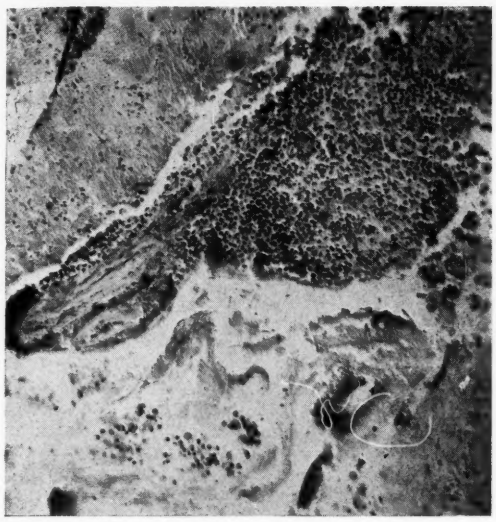

FIG. 130.—*Case* 12. Microphotograph. Tissue removed from sinus in loin (*see text*).

Case 13.—This patient, in addition to having ureteric implants and a scar recurrence, developed a papilloma in his remaining renal pelvis and is therefore dealt with separately in a subjoined article (q.v.).

Case 14.—S. T. McQ., male, aged 46. First seen July, 1933.

Two years and nine months previously (at the age of 44) had had his left kidney removed for "a tumour" by a continental surgeon. Slight transitory hæmorrhage reappeared some months later. For the last nine months has been more or less continuous. No other symptom.

FIG. 131.—*Case* 14. Ureter removed 2¾ years subsequent to nephrectomy. Tightly packed with papillomata, some projecting into bladder. Ureter is short, the upper third having been removed with the kidney.

EXAMINATION.—Weak scar in left loin. Nil else.

Urine: Pink to-day, blood intimately mixed.

Cystoscopy: Bladder healthy. Small clot below L.U.O. A few long, straggling villi project from the L.U.O., but do not completely hide it and apparently do not grow from the lips. Some diathermy to these.

OPERATION (Sept. 4).—Ureterectomy. It was judged that the upper third of the ureter had been taken at the previous operation, the upper end of the stump being reasonably accessible though definitely adherent to peritoneum and muscle.

THE SPECIMEN (*Fig.* 131).—Lower two-thirds of ureter the breadth of a thumb and tightly packed with papillomata. All these are short, but some which were protruding through the ureteric ostium are longer and appear more vascular.

Pathological Report.—Benign papilloma.

PROGRESS.—Recovery uneventful. Regular cystoscopies revealed one papilloma the size of a large pea in January, 1934. Known to be well in 1945.

Comment.—Specimen shows ureter dilated and closely packed with extremely numerous papillomata. The ureter is short, the upper third having been removed at the preceding nephrectomy, which materially assisted the liberation of the upper end of the ureter.

Case 15.—F. H. R., male, aged 50. *Papilloma of renal pelvis with hydronephrosis and stone.*

HISTORY.—October, 1930: Left renal colic and passed a small stone. Similar renal pain, generally mild, till July, 1932, when he had many huge clots with clot retention and much pain.

ON EXAMINATION.—Well-nourished man, 6 ft. 5 in. in height and well proportioned. A large mobile kidney filled most of the left loin and abdomen. Nothing else of note. No varicocele.

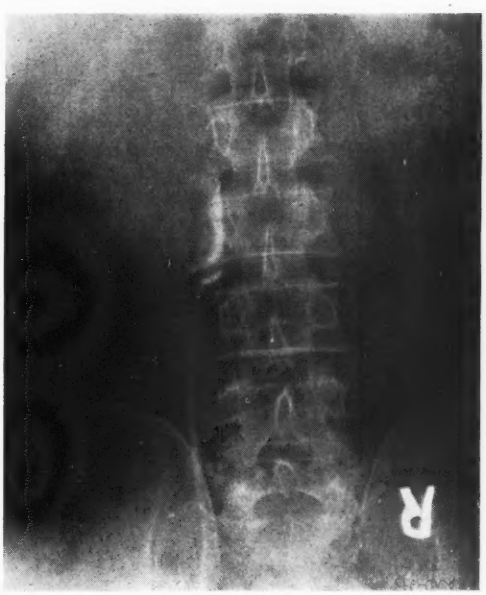

FIG. 132.—*Case* 15. Retrograde pyelogram. Catheter denied entrance to pelvis and fluid outlines only the lowest portion. Pelvis displaced downwards and inwards and evinces a large filling defect.

Radiography: Right kidney normal in size but of elongated type. Left kidney outline easily seen, very large, overlaps spine internally and extends from ribs to below iliac crest.

Spun urine (July 9, 1932): Some pus cells. A few R.B.C.'s and epithelial cells. No casts seen. Film, no T.B. seen. Culture sterile. Sept. 12: Blood-urea 54 mg. per cent.

Cystoscopy (Sept. 7): Bladder of normal capacity, readily clouding. Mucosa clean. Prostatic rim a little prominent. Efflux: R.U.O., clear; L.U.O., muddy. Indigo-carmine: R.U.O., 4–5 min., good; L.U.O., not in 15 min.

Left pyelogram (*Fig.* 132): Catheter passed as far as the ureteropelvic junction. Some fluid passed into

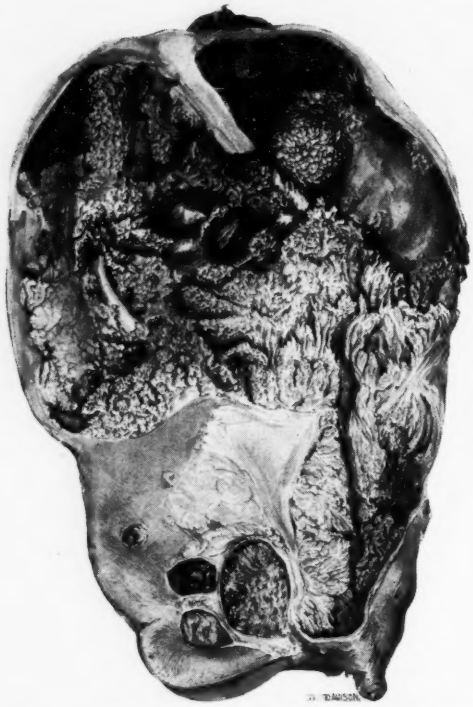

FIG. 133.—*Case* 15.—Enormous kidney packed with papillomata and severely hydronephrotic.

pelvis and mixed with fluid already present. A portion remained near the outlet of the kidney and showed clear

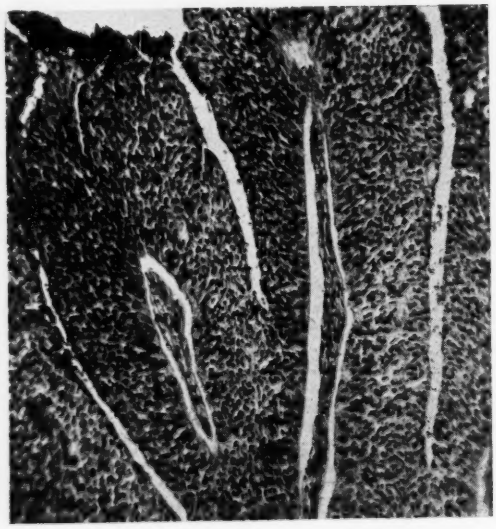

FIG. 134.—*Case* 15. Microphotograph. Benign papilloma of pelvis.

internal margin, but external margin was encroached upon and calices were obliterated. Shadow overlies spine.

OPERATION (Sept. 13).—A large tense kidney could not be delivered into the wound. Trocar and cannula inserted into kidney and approximately 50 oz. of thin, purulent, and blood-stained fluid were withdrawn and thereafter the kidney was brought up into the wound. Nephrectomy (*Fig.* 133). Only after the operation, on incising the kidney, was the nature of the specimen realized and the ureter had then been left behind. Ureterectomy was discussed, but the patient decided against it.

Pathological Report.—Benign papilloma of the pelvis (*Fig.* 134).

FIG. 135.—*Case* 15. Ureter belonging to kidney shown in *Fig.* 133. Removed 4½ years later.

Feb. 24, 1933: Re-examined, well. Weight recovered. External examination negative. Seen periodically for 2 years.

Spring, 1937: Returned with hæmaturia. Papilloma size of small plum completely hiding L.U.O. Benign appearance. Long tenuous fronds. Three sessions of diathermy served for its destruction. When the bulk was gone a papilloma originating within the ureter alternately protruded and retracted with respiration and ureteric peristalsis. Some gentle intramural diathermy.

July, 1937: Ureterectomy. Removal in one piece unopened (*Fig.* 135).

March, 1938: A single but unmistakable frond at L.U.O. Touched with diathermy. Otherwise well.

November, 1946: Reported well. Some hyperpiesia.

Comment.—

1. Pyelogram shows displacement of the kidney and failure to fill and nothing characteristic of a pelvic tumour.

2. Secondary ureterectomy was refused. Symptoms of ureteric tumour delayed till 4½ years, when a diseased ureter was removed.

3. A very large hydronephrosis was present and was tapped. This was necessary but is eminently undesirable, because of the possibility of wound contamination. Fortunately no ill resulted, the patient being well after 16 years.

Case 16.—A. L. McC., male, aged 64. *Papillo-carcinoma of the renal pelvis.*

HISTORY.—Hæmaturia, Christmas, 1936, painless, 5 days. Again in February, 1937. During spring and summer of 1937 urine generally hazy or smoky.

Previous medical history: Scarlet fever 40 years ago. Rheumatic fever nil. Policy has been loaded because of cardiac trouble.

ON EXAMINATION.—External examination, negative. P.R., nil.

Urine: Healthy, but some excess of Ca oxalate crystals.

Cystoscopy: Healthy bladder. Indigo-carmine: Delayed from R.U.O.

Retrograde and excretion pyelograms: Show cutting off of lowest calix and lowest portion of the pelvis. Crenated upper margin (*Fig.* 136).

OPERATION (November, 1937).—Nephrectomy with 6 in. of the ureter.

SPECIMEN (*Fig.* 137).—Large papilloma of the lowest calix with destruction of some of the renal parenchyma of the lower pole. The attached ureter is not affected. A cyst of moderate size is present in the internal border of the upper pole.

Microscopy.—The histological pattern of the fronds is excellent and there is an absence of mitotic activity (*Fig.* 138).

of neoplasm or dilatation in that part of the ureter which had been removed, and by the satisfactory histology.

Continued well till Nov. 4, 1941, when he reported hæmaturia.

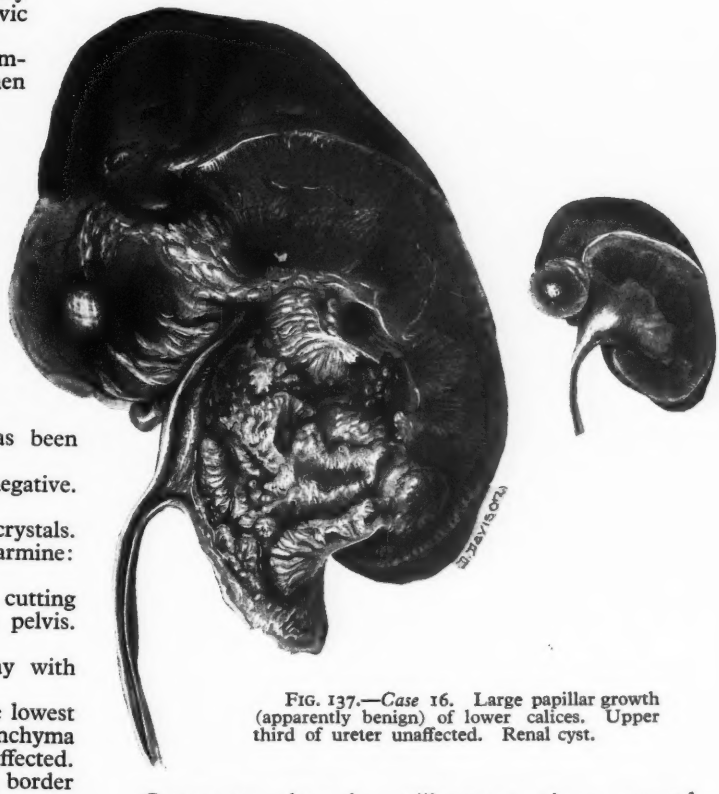

FIG. 137.—*Case* 16. Large papillar growth (apparently benign) of lower calices. Upper third of ureter unaffected. Renal cyst.

Cystoscopy showed papillomatous tissue around L. U. O. Diathermy to the bladder growth and removal of a remnant of ureter (*Fig.* 139). Several cystoscopic diathermies without improvement. Tumour the size

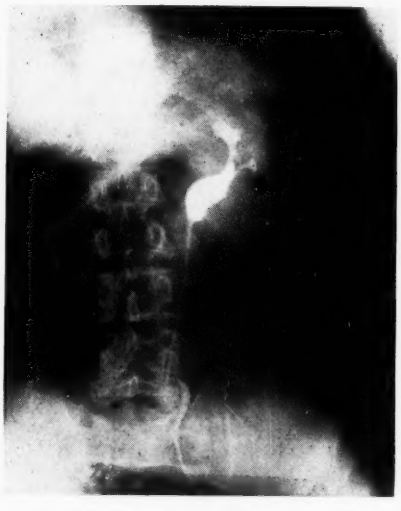

FIG. 136.—*Case* 16. Retrograde pyelogram. Obliteration of lowest calices—closely mimics a parenchymal growth of lower pole.

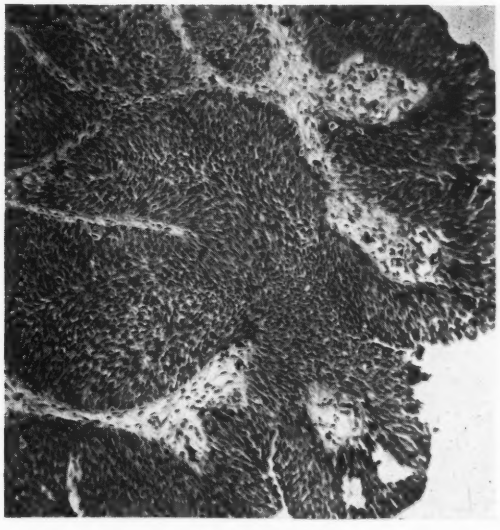

FIG. 138.—*Case* 16. Microphotograph. Apparently benign papilloma of renal pelvis.

PROGRESS.—Consultation with physician regarding advisability of completing the ureterectomy in view of the general health. It was decided that this was contra-indicated and this opinion was supported by the absence of half-a-crown. Obviously infiltrating. Hæmaturia off and on.

May 13, 1942: Referred to Christie Hospital for deep X-ray therapy. Tumour dose, 3740 r. Time, 9 days.

About this time some hæmoptysis occurred and X-ray examination of chest showed metastases.

Died Sept. 17, 1942, with evidence of secondaries in lung, scapula, and ribs, Bladder gave no further trouble.

Comment.—

1. Pyelogram shows a picture indistinguishable from that of a parenchymal carcinoma.

FIG. 139.—*Case* 16. Ureter. Malignant recurrence in ureter (*see text*).

2. The papillomatous nature of the growth was not recognized till after the operation and only the upper ureter was removed.

3. Reasons for not recommending a further operation: (*a*) Policy loaded (cardiac); (*b*) Long segment of upper ureter was healthy; (*c*) Pathological report benign.

4. Though sections taken from the kidney were essentially benign, the recurrences in the bladder were markedly malignant. Dissemination widespread, showing unreliability of the pathological report.

5. Bladder quiescent after deep therapy for several months.

Compare clinical course and pathological reports of the case in which two growths of different pathological types occurred in the same kidney (*see* succeeding article).

Case 17.—This patient is of special interest as, in addition to a papillo-carcinoma of the pelvis, she had a (parenchymal) tumour of the same kidney. She is therefore made the subject of a separate article (*see* p. 134).

Cases 18, 19.—These two patients were process workers in an aniline dye manufactory. They are therefore dealt with in a succeeding article (*see* p. 137).

PATHOLOGY

The epithelium of the urinary passages, structurally unparalleled within the body, gives rise to tumours which are in many respects likewise unique. As clinicians our classification of these tumours should be a strictly practical one. The primary grouping is into the villiform or papillomatous, and the solid or non-papillomatous growths, a classification which is valuable as the clinical behaviour of the two groups is different, This paper deals only with the papillomatous types which are distinguished by their peculiar mode of spread to subjacent parts (in the present series 7 cases show spread to the ureter and 6 to the bladder), a feature not shared to any extent by the solid growths. The papillomata are also less malignant than the solid tumours, which are characterized by extreme malignancy. Numerically the papillomatous tumours exceed the solid varieties by about 3 to 1 in the general literature (Swift Joly, 1933*).

The *papillomata* are further subdivided by most authors into benign and malignant. The question whether this is justifiable is a vexed one. Though it is easy to state positively on microscopical, and often on naked-eye appearances, that a given tumour is indeed malignant, in asserting that an apparently benign tumour is in fact benign we are on much less safe ground and not a few observers have denied that such a thing as a truly benign papilloma exists. For a papilloma to be malignant it is not necessary that it should be invasive, and in fact some authors have subdivided these tumours as: (1) benign, (2) malignant—non-invasive, (3) malignant—invasive; and this classification has the advantage of being useful in practice, though possibly not pathologically sound.

In the first group the stroma is regular and the villi are delicate though rarely long like those seen in the bladder. The cells are well-formed and orderly in their appointed layers, which correspond with those of the strata from which they sprang.

In the second group the stroma is retained, though sometimes showing round-cell infiltration. The villi tend to be shorter, but it is to their epithelial covering that we look for slight but suspicious alterations. Orderliness is less pronounced, the shape, size, and staining properties becoming erratic. The layers may be increased in numbers and vacuolation is sometimes seen. The nuclei share the irregularity and mitotic figures betray increased activity.

The borderland between the first and second groups is ill defined. In it the structural differences are trifling and easily missed, which accounts for many discrepancies in pathological reports.

In the third group, infiltrating papillomata, these tumours have, of course, an invasive part but the prominence of the tumour repeats the features

* Papillomata, benign	120	
,, malignant	138	
		258
Transitional-cell carcinomata	29	
Squamous-cell carcinomata	50	
		79
		337

of the second group which, however, tend to be better marked and less elusive, though this is not always so.

There is a general concensus of opinion that the papillomata of the renal pelvis and ureter are more highly malignant than the corresponding tumours of the bladder.

The following facts are beyond question—it will be noted that the majority have their counterpart amongst the papillary tumours of the bladder :—

1. A papilloma may be benign in one part and malignant in another, A good example is *Case* 17, where the first sections cut appeared satisfactory but amongst the further sections was one showing the definite cytological changes of malignancy. It is a practical impossibility to be sure that every portion of a large growth has been examined so that no carcinomatous area has been missed. The cancerous inclusions are often minute (Kümmel, 1925).

2. The tumour may be reported benign by a pathologist and yet clinically behave as a carcinoma. Presumably in such a case a focus of malignancy has escaped observation. An example of this is seen in *Case* 16.

3. The reverse of (2) may occur, the report being unfavourable and the post-operative course satisfactory (*see Cases* 2, 9). This obviously may simply represent the triumph of surgery.

4. The primary growth may be benign and the satellites malignant. This is an alternative explanation for *Case* 16.

5. The reverse of (4), the primary being malignant and the satellites benign, as in Drew's case (1896). This is much more uncommon and I have not personally witnessed such a combination.

6. A growth may be benign in its early stages but become malignant later. This appears to explain *Cases* 2, 3, in which there is respectively a 9- and a 12-years' history of hæmaturia. Particularly in the latter, the growth, which is of quite modest dimensions, could not have been malignant through all these years and has probably undergone metaplasia late.

7. Secondary deposits do not necessarily resemble the primary focus. Thus in Haslinger's patient a papillary carcinoma of the renal pelvis gave a squamous-cell carcinoma in the ureter. A similar metaplasia has been recorded by Beer in the deposits in the lymph-glands.

8. The change from benign to malignant when papilloma cells have been released in cellular tissues has been discussed at more than one point in this paper and several illustrative and instructive cases are presented (e.g., *Cases* 12, 13). Whenever papillomatous material is implanted in a wound, whether the growth in its original situation be benign or malignant as appraised clinically and pathologically, the implant will behave as a malignant one.

The writer believes that implants are always transferred with the stream of urine, never from below upwards, so that transference from a primary focus in the bladder or ureter to the kidney does not occur, as has been assumed by some writers. An exception, however, is evident in a hydronephrosis where the shed papillomatous implants fall back into the dilated calices and take root.

SYMPTOMS

Hæmaturia.—With these growths the triad of cardinal symptoms—hæmaturia, pain, and tumour—obtains much as with other tumours of the urinary tract. The impression nevertheless remains that *hæmaturia* dominates the clinical picture. It was present in every case, but varied from " a few flakes " to a severity necessitating immediate transfusion. At the one end of the scale stand two such exsanguinated patients (*Cases* 2, 4); at the other the two dye workers in whom the bleeding could not be detected apart from laboratory investigation. These latter, however, developed hæmaturia subsequently. Two women gave excessively long histories, the one 12, the other 9 years, but these are unusual, an average time being a few weeks to 18 months. The shortest history was 3 days (*Case* 11).

Clot colic, with or without the passage of pencil-like clots, was noted in several instances. One patient (*Case* 12), whose kidney had already been removed and who had ureteric secondaries, made the observation that his urine was liable to be heavily stained on one passing and perfectly clear on the next, discomfort in the side being an occasional accompaniment of the blood-free interval. A second patient (*Case* 3) stated that if pain was present clots were absent and vice versa.

Pain.—In these pelvic tumours pain was but little in evidence. There are only two in whom the onset symptom was not hæmaturia. In *Case* 15 colic, probably explained by the passage of a small stone, preceded the onset of hæmaturia by two years. In the intervening period mild renal pain persisted. In *Case* 11 left-sided colic was preceded by homolateral epididymitis. Hæmaturia appeared later.

Tumour.—Of the 19 cases three came to me having been nephrectomized and it is not known whether a tumour was observed prior to that operation. One of these cases, however, appears in this list, for he developed a tumour in his second kidney. There are thus 17 cases, of which 11 showed no lump on clinical examination.

A tumour in the loin is generally said to be caused exclusively by a hydronephrosis (or hæmato-nephrosis). That this is not true can be shown by an examination of my notes. An enlarged kidney is recorded six times. In three of these the neoplasm constituted the lump, of which two were exceptional papillomatous growths in dye workers and the third was a simple papilloma confined to the pelvis and of only moderate size. In two cases a tumour and hydronephrosis were, in combination, responsible for the renal enlargement, and only once was the swelling solely hydronephrotic, the growth being a small carcinoma obstructing the ureteropelvic junction.

A diagnostic point is that a hypernephroma rarely, if ever, causes a hydronephrosis; the lump is the tumour itself, so that if, where a tumour is suspected, we can by pyelography or otherwise show a hydronephrosis, that is evidence in favour of a pelvic origin for the growth. The trouble may be to demonstrate the hydronephrosis.

SPECIAL INVESTIGATIONS

Cystoscopy.—In this series of 19 cases 15 were cystoscoped as a diagnostic measure. We have no records of the remaining 4 cases, either because they had had a nephrectomy elsewhere or for various other reasons given in the appended case histories. Amongst these 15 cases there are 2 in which the first investigation failed to reach a satisfactory diagnosis and one or more additional cystoscopies were required. These patients were sent home, to report immediately the bleeding returned. One came back in five months (*Case* 6), but a delay of three years occured in the case of the small girl aged 12 years (*Case* 10) whose specimen is lent me by Mr. Newell. This child had been seen when 9 years old (the age incidentally is interesting) at another hospital and no diagnosis had been made. When she first visited Mr. Newell bleeding had ceased and she was sent home " with instructions to her parents to bring her back immediately there was another attack. This they did three times, but each time the hæmorrhage had ceased. It was on the fourth occasion . . . that a cystoscopic examination revealed blood spurting from the right ureter."

It is remarkable that of these 19 cases only 1 case (*Case* 3) showed new growth in the bladder at the first cystoscopy, this being a carcinoma with obvious vesical infiltration at the first visit. One showed slight cystitis and several of the elderly males a minor degree of prostatic hypertrophy. In *Cases* 2 and 4 where exsanguination was a feature the extreme pallor of the bladder was remarked. Otherwise there was no vesical disease.

Post-operative recurrences in the bladder have been observed five times. Three reacted satisfactorily and permanently to diathermy, the two others were infiltrating carcinomata which played at least a contributory part in the death of the patient. In the two dye workers, whose histories are recorded in the succeeding paper, papillomata of the bladder appeared four and five years respectively *before* the pelvic growth was recognized, and the condition in each is regarded by the writer as an example of multiple primary tumours. In 2 cases ureteric secondaries were visible, the fronds projecting through the ostium in one (*Case* 14), and in the other (*Case* 15) three sessions of diathermy served to destroy a vesical papilloma the size of a small plum. " When the bulk was gone a papilloma originating within the ureter alternately protruded and retracted with respiration and ureteric peristalsis." Eventually such a growth rubbing against the lips of the ureteric mouth will engraft itself there. The orifice will soon be hidden and there is considerable danger that the vesical growth will be regarded as the primary one and that it will be treated without respect to the parent tumour. Recurrence will then take place early and repeatedly. This has happened in the experience of many writers. A routine excretion urogram might obviate this mistake.

The Ureteric Efflux.—The first cystoscopy revealed a bloody efflux on 5 occasions, in two of which it was described as profuse. In one patient (*Case* 4) whose kidney subsequently proved to be hæmatonephrotic " a tarry stream mixing slowly with the bladder contents " was recorded. A lazy stream of altered blood of this description strongly suggests a functionless blood-containing sac such as was discovered here. The lips of the ureter are sometimes stained from the previous passage of blood (Fenwick's sign).

Repeat cystoscopies, rendered necessary by the failure of preceding cystoscopies, discovered blood from the ureter twice, once on a second (*Case* 6) and once on a fourth (*Case* 10) examination. One patient from whom a kidney had been removed elsewhere was referred to me when bleeding recurred, and at cystoscopy " a worm-shaped coagulum was in process of extrusion from the left ureteric orifice ". This patient (reported elsewhere) developed a papilloma in his remaining kidney four and a half years later, blood then being seen emerging from the right ureteric orifice.

In one patient (*Case* 15—a large renal papilloma) the efflux was " muddy and the bladder contents readily clouded ". This efflux was non-purulent. In fact, there is no example of a grossly infected kidney or bladder in this series. Sepsis is frequently remarked in the literature, but the papillomata, though far from immune, are much less susceptible than the solid tumours of the pelvis.

Renal Function Tests.—The indigo-carmine test was used throughout and proved itself extremely valuable not only as an indicator of the severity of the renal damage but also as a pointer to the side of the disease. It was absent on the affected side in 5 cases and in an additional 5 there was delay, varying from 1 minute to 12 minutes and constantly associated with relative weakness of the coloration. Only in one patient was there no recognizable alteration in the efflux (*Case* 6).

The strong contrast between the rich blue of indigo-carmine and the red of a blood-stained efflux is fortunate. The assistance obtained by me contrasts sharply with the experience of Thomas and Regnier. Using phenolphthalein, they stated that they were " unable to do a satisfactory differential functional test in any of our cases".

Pyelography.—Not a few writers on renal pelvic tumours have been inclined to belittle pyelography as a diagnostic measure in this disease, saying that it generally proves unhelpful. Whilst admitting that this may in some instances be true, the author claims that an examination of the pyelograms now presented shows that its assistance is anything but negligible, that, in fact, it often provides indispensable evidence of a tumour's presence and not infrequently displays its features in detail. The picture, however, varies considerably from case to case and a number of situations require consideration.

1. When the growth is *very small* it will be unrecognizable by pyelography. Even at this stage it is capable of bleeding copiously and persistently though minor hæmorrhages with long periods of freedom are the rule. Two cases in this series illustrate the difficulty of diagnosis at an early stage, either by pyelography or otherwise, and my practice has been to instruct such patients to report immediately the hæmorrhage returns, a cystoscopy then being carried out promptly. An example of a minute papilloma giving rise to hæmaturia persisting for about nine weeks was published by Anderson (1929).

The papilloma lay in a calix and was so small that it almost escaped detection when the kidney was laid open subsequent to operation.

2. *Obstruction* to the urinary passages will arise sooner or later, but its onset will vary with the position of the tumour. It may be postponed for a long time, as in *Case* 1, where multiple papillomata filled the pelvis and yet caused no obstruction. Most pyelograms in this disease show some grade of pyelectasis and, therefore, indicate a pathological condition though the cause of the dilatation is not always revealed. The distension varies from minor degrees to a hydronephrosis containing some pints of fluid, as in *Case* 15 and *Case* 3.

The commonest situation for obstruction is naturally the junction of pelvis and ureter and examples of this are numerous in the present series. If the seat of the tumour is at or near the junction obstruction will be early and is generally severe (*Figs.* 111, 118), its main cause being the involvement and contraction of the walls of the channel. If, on the other hand, the pedicle lies at some distance obstruction will await the production of a frond of sufficient length to plug the renal outlet.

A growth originating in a calix may soon fill and obliterate the latter (*Cases* 8, 9, 10), but if situated at the pelvo-calicine junction it causes a distension limited to the calix itself, as seen in *Cases* 17, 19.

Blockage of any section of the urinary passages will, if complete, prevent catheterization for the making of a retrograde pyelogram. This happened with several growths at the ureteropelvic junction (*Figs.* 111, 118, 132). Complete obstruction not only to the passage of a catheter up the ureter but also to the introduction of contrast fluids is very suggestive. It has been one of the most valuable methods of making a correct diagnosis in cases reviewed in the literature. But even if the catheter fails it does not necessarily follow that the channel will be impervious to fluids, which may seep past in larger or smaller amounts and prove instructive. Obstruction eventually leads to a dilated and non-functioning kidney and so to absence of any shadow in descending pyelography. In combination, a stricture and a functionless kidney are responsible for the absence of a pyelogram in a high percentage of pelvic and ureteric neoplasms, as by one the ascending and by the other the descending route is debarred.

3. *Filling Defects.*—It would seem that a tumour growing within the pelvis must of necessity encroach on the lumen of that cavity and this is true except for the rare instances in which ulceration proceeds concurrently with growth. The filling defect may, however, be unrecognizable because it is small or because it is lost in the deep shadow of a hydronephrosis (*Case* 4).

Filling defects, when present, may or may not be distinctive. Some of them, especially when the neoplasm abuts on the parenchyma or has invaded it, completely cut off a piece of the pelvic outline, generally one or other pole (*Fig.* 136) and such pyelograms are usually indistinguishable from those produced by a renal carcinoma (hypernephroma), though sometimes a brush-like edge suggests frond formation.

The most distinctive and valuable of all pyelographic pictures is that of a filling defect isolated from the external, calicine boundary of the pelvis so that one can be assured that it is not part of a parenchymal tumour. Several instructive examples of this condition are to be found amongst the pyelograms here reproduced. In *Figs.* 121, 142 A, B isolated, rounded defects are unmistakable and there is a suggestion of a crenated margin. In *Fig.* 143 the line of the upper calix is broken by something projecting into the cavity from a place where the only possible origin is the pelvic wall. The irregularity of the free border is also significant. (*Fig.* 147, p. 139, is also noteworthy.) Filling defects are, as a rule, more clearly seen in retrograde than in excretion pyelograms but may nevertheless be quite satisfactory in the latter (*Figs.* 121, 142, 147). The possibility that they result from some cause other than a tumour must be ever present in the surgeon's mind, but the alternative causes—especially blood-clots—are generally transient and can be excluded by repeating the pyelogram at a subsequent date.

When the pelvis is completely filled with growth it will, in all probability, admit of neither ascending nor descending pyelography. It will receive little or no contrast fluid introduced by a catheter and a few erratic shadows thrown by small quantities of solution which have penetrated amongst tightly packed villi is all that should be expected (*Figs.* 118, 132). A tumour of this description will have compressed, invaded, or otherwise destroyed the renal parenchyma, so that no excretion pyelogram is available.

A bulky tumour of the upper pole causes downward displacement of the body of the gland and a large lower pole throws the ureter inwards towards or over the spine exactly as a tumour of the parenchyma does (*see Figs.* 111, 132).

Ureterography.—This has not proved itself valuable in diagnosis of *secondary* ureteric involvement, though widening of the channel and an irregular line might be expected. When a previous nephrectomy has been followed by continued hæmorrhage, the bladder being clear, the diagnosis is self-evident and ureterography is not called for. Thomson-Walker (1929) " tried by passing a catheter up both ureters and working it in the ureter to produce hæmorrhage sufficient for a diagnosis, but failed to obtain blood." To the present writer this appears unnecessary and injurious. Growths which are *primary* in the ureter are in a different category, as they tend to produce obstruction which is more pronounced and ureterography is more helpful.

STONE

In two of my cases (*Cases* 2, 4) stones were observed and in a third (*Case* 15) the patient himself reported the passage of a small stone, but as no medical man saw it the history must be regarded as unreliable. Evidence of urinary lithiasis, whether on the radiograph or otherwise, gains importance from the fact that it confuses the diagnosis, the much commoner stone disease being held to explain the whole clinical picture and the neoplasm being excusably overlooked.

That a very definite relationship exists between stone formation and the growths of the renal pelvis

is unquestionable. Many collectors of statistics have drawn attention to this association, but figures vary widely from those of Stüsser, who found 7 stones in 11 tumour cases (63 per cent), to Rousselot and Lamon (1930), with 6 stones in 49 (12 per cent). The figures of collected groups are difficult to interpret because the same cases appear in several different lists so that the lists must not be added together and an average struck. As regards the association with stones an attempt to separate in the literature the papillomata from the solid tumours has failed and the ensuing discussion concerns both categories, it being, however, acknowledged that stone is definitely more frequent amongst the solid carcinomas than amongst papillary tumours. Voelcker and Boeminghaus (1927) estimated that the solid tumours were complicated by stone in 40 to 60 per cent of cases. Stone is more common with pelvic than with ureteric growths, from which it might be argued that *irritation* of the lining membrane is a factor.

The epithelium of the urinary passages is called transitional because, though markedly stratified, it shows little disposition in ordinary circumstances to undergo keratinization or become horny. Yet when irritated it is capable of keratinizing and the resulting condition, *leucoplakia*, is perhaps best seen on the exposed mucosa of an ectopia vesicæ. Here it is known to be the precursor of malignant growths. In contact with stones or chronic infection in the bladder and renal pelvis the transitional epithelium likewise becomes leucoplakic and this predisposes to the development of a carcinoma, usually of the squamous variety. Of 19 tumours of the renal pelvis collected by Spiess (1915) leukoplakia was discovered in 3 cases.

It is suggestive that something like 50 per cent of all squamous tumours of the pelvis are found in association with stones.

If one takes the trouble to examine reports in the literature, mostly of isolated cases, one can scarcely fail to be impressed by the length of time some patients with an association of stone and carcinoma have had symptoms. To quote only three examples :—

Wilfred Adams (1937).—
Hæmaturia 30 years previously, massive calculi. No infection—dense scirrhous growth of the pelvis, epidermoid carcinoma.

Kenneth Walker (1934).—
Hæmaturia 29 years previously. Squamous carcinoma of the pelvis. No infection. Multiple stones, uric acid and calcium oxalate.

S. J. Waterworth (1932).—
Discomfort right abdomen 30 years ago. Severe hæmaturia 28 years ago. Stone pure calcium phosphate (2·42 lb.). Squamous carcinoma of the pelvis.

In each of the above it is obvious that the carcinoma, a rapidly growing type, is a newcomer and the presumption is well founded that the calculous disease caused the original symptoms. Stone is, therefore, the precursor in at least some instances in which the two conditions are coexistent.

Infection also plays an important role. It is reported by many writers as complicating a growth. The stones may, therefore, be of the secondary, infective, phosphatic variety, especially where the outlet is obstructed. In this event the growth would be the precursor, the stone the sequel; so that it appears clear that the primary factor is in some instances the stone, in others the growth. These secondary concrements may, of course, form around solid elements, such as portions of detached tumour (therefore more usually papillomata), a process well recognized in bilharzial disease.

That *stagnation* is not in itself a major agent may be surmised from the smaller prevalence of stones with ureteric than with pelvic growths, obstruction being more pronounced with the former. On the other hand it may be argued that the obstruction is earlier and more acute in the former and so probably allows less time for the development of a stone.

That *bleeding* is not an important cause of stone formation seems to be established by the fact that tumours of the renal parenchyma, which bleed just as freely as the pelvic growths, are associated with stones in a much lower proportion of cases (6·2 per cent—Tuffier and Bréchot, 1911).

The stones observed in my two cases were both of the primary type and infection as a cause can be ruled out. In one case two rough, irregular, flattened calculi lay free amongst the fronds and not much significance was attached to their presence. In the other a stone (*Fig.* 116), the size of a marble, occluded the renal outlet, giving rise to so severe a grade of pyelectasis that the kidney was reduced to a mere fibrous shell. A papilloma the size of a grape, and showing much mitotic activity, was judged to be a later lesion, as the marked changes in the kidney were certainly more old-standing than the tumour itself. Leucoplakia was looked for but was not found.

TREATMENT

Reading through the literature one finds that some strange operations have been employed for papillomatous disease in the past. Amongst these are perurethral fulguration of a polyp protruding from the ureteric meatus, transvesical removal of the lower end of the ureter, removal of a length of the ureter with restoration of the canal or with implantation of the upper end into the bladder or on the skin, according to the circumstances. These procedures are mentioned merely to condemn them. Perhaps the rarity of the condition, which limits the experience of individual surgeons, is responsible for such inappropriate methods. In the more recent literature nephro-ureterectomy in one stage is becoming generally accepted as the ideal treatment, a view which is based on the repeated failure of lesser measures to eradicate the disease. If this is impossible, as not infrequently happens, either because the patient is feeble or because of a failure in diagnosis, the operation should be completed at a second stage. This operation is suitable wherever the tumour first shows itself. If it is found in the lower ureter it may be primary, but, as pelvic papillomata are approximately five times as common as ureteric ones, and as they produce seedlings in 40 to 50 per cent of instances, it is evident that the chances are in favour of any tumour in the lower ureter having a parent growth higher up. The kidney must, therefore, be sacrificed with the ureter. If, on the other hand, a tumour is diagnosed in the

renal pelvis the known prevalence of multiple satellites demands the removal of the ureter. The indications are, therefore, simple—wherever papillomatous disease presents itself within the upper urinary tract the ideal treatment is nephro-ureterectomy, preferably as a one-stage operation.

A few observations on the operation itself are called for: The writer employs separate incisions for the renal and ureteric parts of the operation. Some surgeons formerly made a single long incision but the great length of this is objectionable as leading to weakness of the abdominal wall. The bridge of tissue remaining between the separate wounds is not small and is an invaluable post-operative support to the parietes. The lumbar nephrectomy follows standard practice and will not be discussed. Should the renal operation precede the ureteric, the kidney, when free, is, if large, brought out of the lower angle of the wound and the remainder of the wound closed. If small, the kidney can be tucked down towards the iliac fossa pending the pelvic part of the operation.

A review of the literature shows that opinion is divided regarding the relative merits of the inguinal and the paramedian or pararectal incisions for the ureterectomy. The writer recommends an inguinal approach. An incision starting at the pubic spine runs upwards and outwards, following the line of the fibres of the external oblique muscle. When exposed the fasciculi of this muscle are split longitudinally and the deeper muscles are divided in the same line. The incision should be a generous one. It is fundamental that the work to be done, deep in the pelvis and at the upper end, should not be cramped. Nevertheless, some writers speak of a small incision. The author rejects this out of hand. The great advantage of the oblique approach over the paramedian is that the 'bag' of peritoneum requires less mobilization and retraction. It gets in the way to a smaller degree and the operation is thus easier. The approach to the ureter is more direct and is facilitated at the all-important upper and lower ends. No failure of satisfactory healing need be feared nor any hernia formation.

Shall the kidney or the ureter be first attacked? This is not a vital matter assuming that the whole operation is certain to be completed, but the very human anxiety to get final confirmation of the diagnosis—and the diagnosis in some of these cases is necessarily only a provisional one—will probably lead to that part of the channel being approached first in which the principal or primary disease lies, the ureter with ureteric, and the kidney with renal, growths. From a feeble subject with a pelvic tumour the diseased kidney may be removed as a first step and the ureter deferred to a secondary operation, but in similar circumstances with a primary ureteric growth the full operation should, if at all possible, be carried out. If this were deemed unjustifiable the surgeon should consider the desirability of removing the kidney first, leaving the actual ureteric tumour for the second operation, thus avoiding a ureteric ligation which is highly objectionable. If the kidney is grossly enlarged it will, after it has been freed, prove itself an embarrassment during the turning over of the patient and the ureterectomy. With such a mass, whether hydronephrotic or neoplastic, the writer prefers to let the ureteric precede the renal operation. Everidge (1940), however, makes the valid point that "it is simpler and quicker to transfer the patient on the table from the lateral to the dorsal posture, than vice versa".

A bladder which has been completely emptied at the start of the operation facilitates the exposure of the terminal ureter. When the peritoneum has been stripped back from the parietes the ureter is easily mobilized. In none of my cases did adhesions give rise to operative difficulty (except at the upper divided end of the ureter in a secondary ureterectomy —*see* later). Occasionally, however, the ureter has been reported by other writers as densely adherent to the overlying peritoneum and intraperitoneal structures and requiring great care in its removal. Instances have also been reported of its being intimately adherent to the common and internal iliac vessels. The adhesions are said to be more pronounced when radium has been employed. (Day, Fairchild, and Martin, 1925.)

The importance, already emphasized, of avoiding contamination of the wound by particles of tumour requires special precautions at the point where any section of the tract is to be made. Most accounts of the operation performed make no point of *how* the ureteric division was carried out. In most cases the ureter was "clamped and divided", some descriptions adding that it was carbolized, which, of course, is totally inadequate. The inference is that in but few cases was this part of the operation adequately carried out. A glance at such ureters as those shown in *Figs.* 129, 131, 135, 139 will immediately demonstrate the impossibility of dividing the tube without going across papillomatous material. In a one-stage ureteronephrectomy there will be only one point of section—at the entry of the ureter into the bladder. After painstaking exposure of this point and full mobilization, two artery forceps are applied as close as possible to the bladder. A gauze pack is slipped in underneath them to protect the surrounding structures and the division is effected by means of the high-frequency needle, all exposed tissue being *completely* destroyed and the needle being applied to the forceps themselves so as to destroy the wall within their grasp. This procedure accounts for all the ureter, excepting only the intramural section which is now a mere shallow crypt. With benign papillomata this can be safely dealt with by per-urethral fulguration.

This point I feel it incumbent on me to labour even at the risk of becoming tedious. The intramural ureter is the trouble. Seedlings are in this section perhaps more frequent than in any other part of the ureter. To remove it many surgeons (van den Branden, 1933, enumerates 33) have advised the removal of a button, cuff, or collar of bladder surrounding the orifice. This has been called a total ureterectomy in contradistinction to the removal of the ureter down to its point of entry into the bladder wall—juxtavesical or subtotal ureterectomy.

Now it cannot be sufficiently emphasized that loss of a single papilloma cell in the connective tissue will almost certainly entail a malignant local recurrence. The removal of a cuff or collar, or indeed any opening of the passages (but particularly a dependent one), is fraught with extreme danger, for some quantity, however small, of the vesical contents

must escape, and after the operative manipulation of the ureter the bladder contents must of necessity be particularly rich in papilloma cells. Recurrence may be delayed for a considerable time and its relationship to operative contamination may thus be lost sight of. Removal of a collar has been condemned in tuberculous disease as not satisfying the ideal of a closed operation (Everidge, 1940). Why then is it recommended in papillomatous disease, where the danger is so much greater even if less immediate?

The incidence of recurrence in the scar may be judged by the investigations of Makaschew and Sokolow (quoted by van den Branden, 1933). These authors found recurrences in the scar in 33 per cent of 163 nephrectomies (*see* p. 131). This contrasts strongly with the author's almost complete immunity from scar implantation when what he considers to be a correct technique has been used. Yet the opening of the bladder is widely advocated. Amongst others Hunt has recommended it and has been much quoted in America, as, for instance, by Hinman (1935), who, in his excellent *Principles and Practice of Urology*, has approved the method and has reproduced Hunt's figures illustrating the technique. Again Day et al. (1925), writing on the frequency of the failure to recognize the nature of the tumour at operation, blame the fact that " the kidney is not split and carefully examined until closure is made " as they imply it should be, quite overlooking the danger of such a procedure. To meet the resulting high incidence of infection in the scar many authors have significantly resorted to the post-operative use of radium or deep X-ray therapy. (Livermore, 1931; Thomas and Regnier, 1924; Mraz, 1924; and others).

At the International Congress of Urology, 1933, I described a procedure by which the lower end of the ureter was cut juxtavesically and the distal segment was elevated and displayed by forceps whilst an electric needle was inserted into its channel to destroy the lining mucosa. Colston (1935) has since described an almost identical procedure. I do not, however, believe that even this relatively simple procedure completely excludes the chance of implantation, which exclusion I regard as the most important precaution in dealing with these tumours, and I have, therefore, abandoned the method in favour of transvesical diathermy to the intramural remnant.

The operation recommended has the further advantage that it is less severe than one taking a portion of the bladder. In my series it carried no operative mortality. By contrast, van den Branden states that total nephro-ureterectomy presents the great disadvantage of being very severe (" *grave* "), " d'entraîner une mortalité opératoire assez grande."

Secondary bladder growths present before operation constitute different problems according to whether they are benign or malignant. A *benign* growth may be dealt with perurethrally if of reasonable size, and this may precede or follow the ureteronephrectomy, the former being preferable in the absence of some over-riding factor such as copious bleeding from the upper urinary tract.

With *malignant* extensions the position is different and several of my cases bear witness to the danger of infiltration, especially around the ureteric orifice. For many of these elderly patients the addition of a partial cystectomy to an already very major operation would turn the scale adversely and it is possible that a nephrectomy followed at a later date by a ureterectomy and partial cystectomy represents the least formidable distribution of the strain.

If for any of the reasons mentioned above a nephrectomy is undertaken as a first stage the division of the ureter will be carried out with precautions similar to those described for the lower end. It is, however, important to ensure that the upper division is made at the lowest possible point compatible with easy working—if practicable at the brim of the true pelvis. Rock-like adhesions have on four occasions in the present series been encountered where the upper ureter has been sectioned and this has had to be dug out in an extremely inaccessible situation. It is desirable to foresee this difficulty and to ensure by a low division that the upper end of the ureter is made easily available within the lower operative field in readiness for the second operation. To deal safely with a ureter which has been cut off at or near its origin a generous inguinal incision such as that described above gives the best access.

All patients who have been treated for papillomatous disease of the upper tract require a regular cystoscopic follow-up, such as is done for bladder tumours, and this is necessary whether or not papillomata have already been seen in the bladder.

Results.—In the literature on this subject it is astonishing how many authors have rushed into print to record a single example of this comparatively rare disease. The interval between treatment and report is usually but a month or two and no further history enlightens us as to the patient's future. Probably in few conditions are the materials for arriving at an appraisement of results more meagre. Swift Joly, whose admirable survey of the subject of tumours of the renal pelvis and ureter for the Fifth Congress of the International Society of Urology is undoubtedly the most masterly account of the disease, says: " I have had great difficulty in arriving at even an approximately correct estimate of the results of operative treatment, as in many cases the record gives no after-history, whilst others were collected too soon after operation to be of real value."

Further it is extremely difficult to compare the lists of various authors, partly because they adopt different pathological nomenclatures and also because some throw all anatomical and pathological groups together, others giving separate lists.

In analysing the results of treatment the papillomatous tumours, which constitute a majority of all pelvic growths, should, of course, be separated from the solid ones, which are generally speaking more malignant, spread to glands and distant organs earlier and more consistently, and rarely if ever detach secondary seedlings to the lower passages.

Two dye workers, on account of their special features, cannot reasonably be studied in the ordinary list and are, therefore, excluded from the statistics. There remain 17 cases for study. In the section on pathology the writer has discussed the difficulty of determining with certainty whether a papilloma is truly benign or malignant. Of the present series 10 are called benign and 7 malignant.

Of the 10 benign papillomata all are alive and well with two exceptions. One patient had bilateral

growths. He survived the appearance of a papilloma in his first kidney 11½ years. The second fatality is a patient who died of a spinal metastasis and the interval between his first symptom and his death was 10 years. It will be noted that these are the two patients who had local recurrences regarded as due to operative sowing. The intervals between their first symptoms and their deaths (11½ and 10 years) show that this disease may prove fatal at a remote time. For the 8 patients still alive the intervals since operation are 2, 3½, 11, 16½, 17, 20, and 23 years; one other patient operated on 29 years ago was followed for 8 years and discharged as cured.

Of the 7 malignant papillomata 1 is alive and well after 6 years; 6 are dead, 1 without operation. There is no operative mortality. Recurrences in or near the bladder were responsible, at least in part, for the deaths of two patients at 1 year 9 months and 6 years. The last-mentioned of these had mestases in the lungs, scapula, ribs, etc., but the bladder recurrence, following deep X-ray therapy, was symptomatically quiescent for 4 months.

One patient died of secondaries in the liver at 2 years, one with a local recurrence died at 26 months, and one is untraced though certainly dead.

In this series 2 cases must be regarded as having had papillomatous material sown in the wound by faulty operative technique. In a further case of papillomatous disease primary in the ureter (and therefore not included in this series), treated at a relatively early period in the writer's experience, the mistake was made of doing a partial cystectomy combined with a ureterectomy and this also resulted in local recurrence and death. The bladder may be and is regularly opened from the front, with suitable precautions, for the treatment of papillomatous disease without undue risk of sowing papillomatous material, but this is scarcely possible from behind. A better recognition by the profession of this cause of death should lead to a material reduction in the mortality rate. Van den Branden mentions a number of surgeons who routinely employ radium or deep X-ray therapy in one form or another after operative treatment. "The object of these authors," he says, "appears above all to be to hinder implantation ('*la récidive*') in the wound. This is justifiable for, according to Makaschew and Sokolow, in 163 nephrectomies for papilloma of the pelvis there were 54 implantations in the wound" (33 per cent). Now, as previously shown, papillomatous material shed in an operation wound, whether the original growth appeared simple or malignant, will invariably behave as a cancer. Therefore, in the series of 163 nephrectomies just quoted a mortality of 33 per cent may be expected from this cause alone. In the writer's series there are only 3 recurrences in the wound and 2 of them are accounted for by operative sowing. The conclusion is inescapable that faulty technique has a profound bearing on the mortality rate. It is also obvious that a malignant recurrence in the scar is not valid evidence that the primary neoplasm was a malignant one.

SUMMARY

The following are the principal facts which emerge from a study of the material presented:—

1. The only unmistakable evidences of a papilloma of the upper urinary passages are: (*a*) Tumour cells found in the urine, the bladder being clear; and (*b*) A papilloma protruding from the ureter as seen cystoscopically. Many renal papillomata are clinically indistinguishable from the commoner hypernephromata. Pyelograms are frequently helpful, showing a characteristic filling defect, possibly with a crenated margin, but often they show only secondary effects, such as pyelectasis. A few cases simulate calculous disease or hydronephrosis. Failing a correct diagnosis, the ureter will not be removed and a ureterectomy will be required subsequently.

2. The correct treatment is ureteronephrectomy, always assuming the patient's condition will permit so large a procedure.

3. If the nature of the disease is known beforehand the passages will not be opened, as papillomatous material would be implanted in the wound, where it invariably takes on malignant propensities, as illustrated by four cases in this series.

4. The terminal ureter is usually more heavily involved than any other part of that tube. It must be cut flush with the bladder and means must be employed to ensure the destruction of seedlings within the intramural ureter.

5. The division of the ureter is made with an electric knife, the clamped stump of the ureter being completely destroyed.

6. It is unwise to remove a disk of the bladder because: (*a*) This materially increases the severity of the operation; (*b*) Vesical papillomata can be dealt with satisfactorily per urethram; (*c*) The fundamental precaution is to guard against implantation in the wound, this being more easily achieved when the section passes through the ureter than when it involves the bladder.

7. A ureteric papilloma may be the primary growth, but is more likely to be a seedling from above. In either event the proper treatment is ureteronephrectomy.

8. Several patients in this series have undergone a secondary ureterectomy. In most instances the upper end of the ureter at the point where it had been divided was firmly adherent in an inaccessible region and constituted an operative difficulty. If the nature of the disease is recognized, and a ureteronephrectomy is contra-indicated, a low division of the ureter makes for better accessibility at a second operation.

9. Some papillomata can be felt through the pelvic wall at operation, giving a curious sensation resembling wet cotton-wool which is characteristic, the pelvic wall being mobile over the growth.

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BILATERAL RENAL PAPILLOMATA: TWO CASES

BY JAS. B. MACALPINE, MANCHESTER

PAPILLIFEROUS disease occurring in both kidneys has been met with at the Salford Royal Hospital twice.

CASE REPORTS

Case 1.—A dye worker, who, five years after suffering from vesical papillomata, developed bilateral renal papillomata. His case is fully reported in the accompanying paper on papillomata of the renal pelvis in dye workers (*see* p. 138).

FIG. 140.—*Case* 2. The specimen consists of the ureter in almost its whole extent. Two growths of similar appearance are seen, the one springing from a point close to the upper extremity, the other from near the lower end. Each growth shows a few ill-developed villi, is about 1–1½ in. in length, and is attached to the ureteral wall by a relatively small base. The body of each tumour lies free within the ureteric lumen, which is moderately dilated.

Case 2.—R. G. P., male. (Not seen by me till 1939, when he was aged 51.)

HISTORY.—1934, hæmaturia. Recurrence at 12 months and 18 months and then more frequently. Traced with some difficulty to the left kidney, and shortly after that severe clot colic on the left side, when on cystoscopy the blood was seen to emerge from that ureter.

Aug. 5, 1936: Nephrectomy by another surgeon and probably the kidney was incised before removal. Did well and put on weight, but in July, 1939, urine was dark and coffee-coloured for a short time; in September bleeding became severe and was continuous for one week.

Sept. 13, 1939: First seen by me. At cystoscopy the urine was heavily stained and a worm-shaped coagulum was in process of extrusion from the left ureteric orifice.

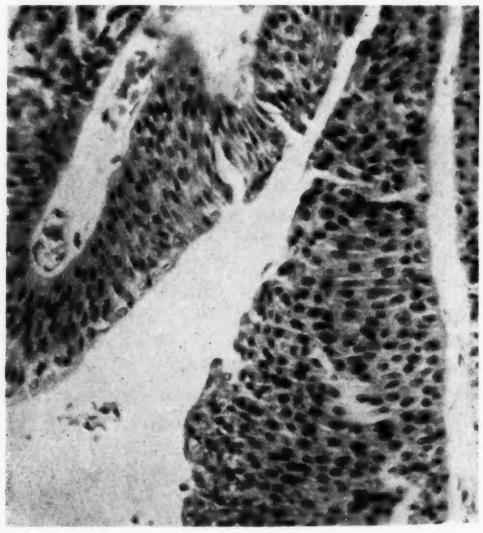


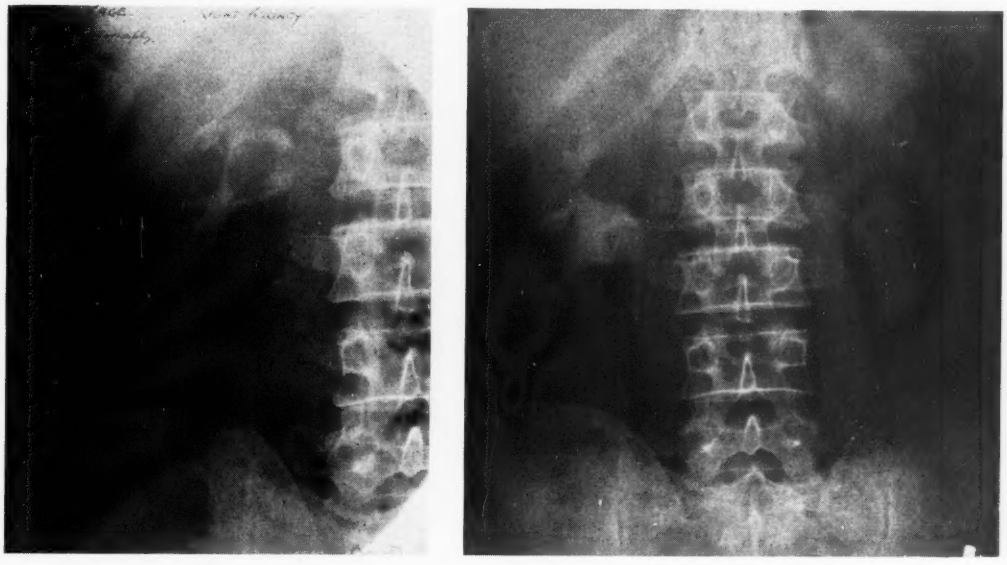
FIG. 141.—A benign villous papilloma, the villi being well formed and the general structure regular with no evident mitotic activity or other indication of malignancy.

Sept. 16: Juxtavesical ureterectomy (*Figs.* 140, 141). Upper end very adherent and buried in a mass of deep scar involving the psoas muscle, colon, and peritoneum. Convalescence uneventful. At subsequent cystoscopies the bladder remained clear.

November, 1940: Pain in back and slight pain in the abdomen, diagnosed (December, 1940) as a local recurrence, an indurated mass being present at the *upper end*

of the kidney scar with central sinus discharging a small amount of blood and pus. Sent to Christie Hospital for irradiation. Tumour dose (X rays) 2350 r. Time, 8 days. Response excellent. (Cf. *Case* 12, p. 120.)

January, 1944: Recurrence of hæmaturia. Cystoscopy showed bladder to be clear, but blood was seen coming from the right ureter (side of the remaining kidney). I.V.P. showed a well-marked pelvic filling defect which was persistent and constant on repeated



A B

FIG. 142.—Intravenous pyelograms. A, Before radiotherapy (May 5, 1944), showing well-marked filling defect. B, After (Nov. 14, 1944), showing definite diminution.

I.V.P. (*Fig.* 142 A). Typical crenated margin. Almost certainly a pelvic papilloma. Very little obstruction.

May 10: X-ray irradiation at Christie Hospital. Tumour dose, 5000 r. Time, 19 days.

Nov. 14: Fresh I.V.P. seemed to show retrogression of the tumour, which was, however, still quite evident (*Fig.* 142 B).

Dec. 23, 1945: Died at home. No details.

DISCUSSION

It is extremely rare to find papillomatous disease affecting each renal pelvis and I have been successful in discovering only 6 other examples. The first of these was reported by Rayer in 1841 and occurred in a woman aged 58 who had abdominal pain and severe hæmaturia. The substance of the kidneys was healthy; on the internal face of the pelvic mucosa were some small pedunculated tumours evidently formed of fibrous tissue, infiltrated with encephaloid material. Similar alteration existed in the ureters. A cancerous mass, formed by an agglomeration of small tumours analogous with the preceding occupied the bas fond of the bladder. They were rounded and incrusted.

In 1870 Murchison reported the case of a man aged 65 who suffered for about three years from hæmaturia. He died in coma shortly after admission to hospital and at a post-mortem examination both pelves were dilated and contained papillomata. There were several papillomata in the bladder, but none in the ureters.

Retzlaff (1904) described the case of a woman aged 53, who was admitted to hospital for an operation on her stomach and died of sepsis and peritonitis. Post mortem, the right kidney was almost completely replaced by a firm, white mass, which involved the pelvis. Microscopically it was described as a medullary carcinoma of pelvic origin. The left kidney contained a similar growth about the size of a bean. This is probably an example of bilateral papillo-carcinomata.

Maybury and Dyke (1925) published the case of a man of 45 who had had hæmaturia for six years. Left lumbar nephrectomy for a large kidney filled with papillomata and hydronephrotic. Section—benign. Nine months after operation recurrence of hæmaturia and the right kidney was found to be enlarged and hard but movable. Provisional diagnosis of papillomata of the remaining kidney was made. Patient too ill for cystoscopy, etc. The renal swelling increased rapidly and became fixed; from it there extended a large, hard, finely nodular plaque, which was adherent to the anterior and lateral abdominal wall and finally reached to well below the level of the anterior superior spine. The patient died three months after the recurrence of the hæmaturia. No sign of recurrence on the left side. No autopsy. Presumption—tumour of remaining kidney.

Sanford (1931) reported the case of a man aged 56 who was admitted to hospital with hæmaturia of two months' duration and also nausea, epigastric pain, and great loss of weight. A full investigation pointed to the right kidney as the source of bleeding, though the left pyelogram showed incomplete filling and a delayed excretion of phenolphthalein. As the hæmorrhage was reaching alarming amounts, the right kidney was removed following a transfusion. Three weeks after the operation the patient weakened and died from uræmia. A post-mortem examination was refused, but the left kidney was obtained. The upper pole of the right kidney "was covered with new growth. A section showed the kidney structure

to be invaded with groups of tumour cells which were arranged in cord-like and alveolar formation. In some areas these cells had a somewhat transitional appearance as though they had originated from the pelvic mucosa. Diagnosis: transitional-cell carcinoma of the kidney originating from the pelvis." The left kidney was the larger of the two and " had its upper and middle thirds entirely replaced by a closely packed mass of carcinoma, the gross appearance of which was wholly different from the scattered nodules of tumour in the other kidney . . . Microscopical section revealed the presence of tumour cells arranged predominantly in a papillary formation. In other areas the structure of the tumour resembled that found in the right kidney. Diagnosis: transitional-cell carcinomata of the left kidney." Sanford says: " . . . with two such advanced tumors it seems impossible for the process in one kidney to have been secondary to the other without finding metastases in the lungs where they are more likely to occur sooner. The short clinical course of the disease (4½ months) and the absence of demonstrable metastases are in favor of a bilateral primary renal carcinoma."

Thomas and Regnier (1924) stated that they had studied 248 case records of tumours of the kidney pelvis and ureter—" we find that tumours of the renal pelvis or ureter occurred in the right side in 53 per cent, the left side in 35 per cent, the [*sic*] bilaterally in 4·2 per cent." No instance of bilateral disease is recorded and no reference is given or other detail, nor do they say what happened to the remaining 7·8 per cent !

Of the two new cases now added to the literature, the one occurring in a dye worker had a known and adequate stimulus to tumour formation to account for the multiplicity of the growths. In actual fact he probably had true primaries not only in each pelvis but also in the bladder, where the disease antedated that in the kidney by several years.

In the second case there is no known tumour-forming stimulus, but considering the extreme rarity of renal papillomata, the chances against any one person getting bilateral growths fortuitously must indeed be high and some unknown underlying biological factor may be postulated, be it a hormone, a special tendency in the individual's mucosa to produce papillomata, or other influence.

The evidence of a tumour in the second kidney of *Case* 2 may in the absence of operative or post-mortem confirmation appear insufficient and be questioned by the purist, but the majority will probably agree that the evidence of the clinical findings, the blood-stained ureteric efflux, and the fatal termination, combined with the characteristic pyelographic changes—consistent in repeated examinations over a period of months—is too strong to be refuted or even challenged.

Of other types of renal new growth, that found in childhood is known to affect both organs in a considerable proportion of cases. Of the renal parenchymal carcinomata (hypernephromata) a small number of bilateral examples have been recorded, the most recent by Hanley (1945), who has collected the preceding cases in reporting his own.

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A CASE IN WHICH TWO DISSIMILAR GROWTHS, AN ADENOMA (ADENOCARCINOMA) AND A PAPILLO-CARCINOMA, OCCURRED IN THE SAME KIDNEY

BY JAS. B. MACALPINE, MANCHESTER

IT IS so exceptional to find two separate tumours of different pathological types occupying the same kidney that such an occurrence is worth recording.

CASE REPORT

Female, age 72. Had had hæmaturia for seven months. Intermittent, but frequently copious. Some bladder pain from minor clot retention. Frequency: day—variable, increased during attacks; night—variable, average of two or three times.

ON EXAMINATION (Sept. 15, 1942).—A feeble patient. Older than her years. Bronchitis. Some emphysema. Myocarditis.

Cystoscopy: Bladder healthy. Blood from right ureter profuse.

Retrograde pyelography (*Fig.* 143): The middle and lower calices show a minor degree of dilatation and clubbing. The upper calix shows elongation and dilatation and a pronounced filling defect which interrupts the sweep of the wall at the pelvocalicine junction and extends into the upper middle calix. The kidney shadow is well seen and of normal size, shape, and position.

DIAGNOSIS.—Papilloma of the upper calix.

OPERATION (Oct. 1).—Nephrectomy, and removal of the ureter to the pelvic brim.

THE SPECIMEN (*Fig.* 144).—Shows a papilloma of the upper calix and a small subcapsular hypernephroma (1 in. by ½ in. in diameter). The ureter is free from growth to the point of division. It is almost certain that the bleeding arose from the papilloma, not from the hypernephroma.

Though a correct provisional diagnosis of papilloma of the renal pelvis was reached, when the kidney was exposed the hypernephroma, which was subcapsular, evident, and quite characteristic in appearance, proved misleading. It was regarded as the responsible lesion. A moderate length of ureter was nevertheless removed. Not until the kidney was opened post-operatively was the papilliferous growth discovered. In view of the feeble state of the patient it was thought to be unwise to complete the ureterectomy. It was decided to await events.

Pathological Report (Professor Baker, Manchester).—"1. *Papillary carcinoma of pelvis of kidney*: Section through a papillary tuft shows the appearance of a transitional-cell papilloma. Another section through a small mass in a calix shows a small solid mass of growth with the cytological changes of a carcinoma—variations in nuclear size and staining and numerous mitoses. The epithelial lining of this calix is thickened and shows in one area the cytological changes of carcinoma. The kidney substance in the region of this calix shows inflammatory changes with focal collections of leucocytes.

"2. This is an adenoma with fatty changes in the epithelium and collections of fat phagocytes. In parts it is like a hypernephroma and is interesting in suggesting the origin of the hypernephroma from tubules but I don't think it has got to one yet. I have had a frozen section done on this and confirmed the lipoid changes in the epithelium."

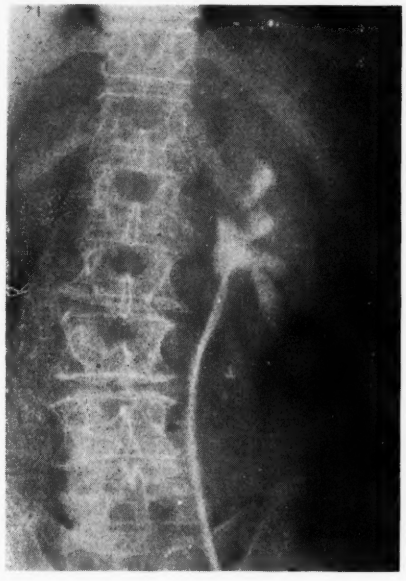

FIG. 143.—Retrograde pyelogram. Filling defect of upper calix, etc., faithfully portraying the pelvic lesion seen in accompanying coloured drawing, *Fig.* 144. (*See also text.*)

Professor Willis, of the Royal College of Surgeons (the specimen has been given to the Museum of the College), gives a similar opinion: "There is no doubt of the distinct characters of these two tumours. The one is a typical papillary growth of the pelvis and the other is an unusually large papillary adenoma or a small carcinoma of the cortex—whichever you please. No sharp distinction can be made between the common small benign adenomas and the larger progressively growing papillary adenocarcinomas, usually referred to by the bad name 'hypernephroma'. There is little doubt that the latter often arise out of the former. In my opinion, this particular specimen is of relatively benign structure, and I would prefer to call it a 'cortical adenoma'."

PROGRESS.—A cystoscopy done routinely at six months revealed no lesion and the patient was in fair health, but bleeding recurred within the year and a tumour was then discovered (Oct. 7, 1943) at the right ureteric orifice and actually growing from its lips. Ureterectomy (*Fig.* 145) was carried out, but fulguration of the vesical growth was unavailing and the patient's health precluded the more radical partial cystectomy.

March 10, 1944: Symptoms persist, with increasing strangury, etc., but the patient's condition does not permit radical treatment and the bladder condition is actively malignant.

June 10: Died at home.

THE SPECIMEN (*Fig.* 145).—The lowest two-thirds of the ureter. It shows a tumour in its upper part, but is curiously free below where the growth might have been expected in view of the neighbouring bladder

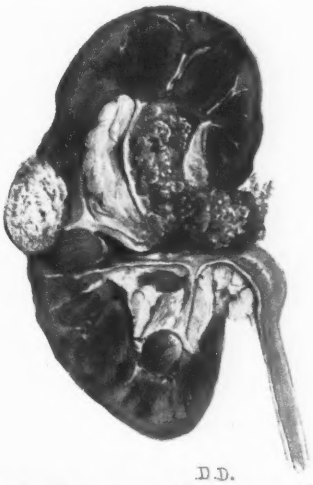

FIG. 144.—Papillary growth of the upper calix combined with a subcapsular adenocarcinoma (hypernephroma). Note absence of ureteric involvement.

involvement. Villi are evident in the lower part of the growth but become less obvious as the upper end is approached. In the middle section the neoplasm is non-villiform, hard, nodular, and infiltrating. At the upper extremity there is actual ulceration. The fibro-fatty

FIG. 145.—Lower portion of ureter, showing malignant papillomatous change (*see text*).

tissue seen around the upper end bears witness to the dense adhesions which form at the point of section of a ureter, to which I have drawn attention elsewhere.

Comment.—In the pathological report on the kidney, the present writer directs attention to the difference in the microscopical characters of the two papillary tumour sections. If a single section had been relied on the malignant nature of parts of this growth might have been

overlooked. This feature brings renal papillary growths into line with those found in the bladder, where a similar phenomenon is well known. It also emphasizes the importance of serial sections, to which Albarran has drawn attention. The possibility of overlooking such an area makes the surgeon wary of ever pronouncing any papilloma benign. A number of writers have, indeed, stated that serial sections of a papilloma always show malignant change at some point.

DISCUSSION

Graves and Templeton (1921) recorded 2 cases of combined tumours of the kidney which are relevant to the present discussion.

A man, aged 52, had seen blood in his urine intermittently for a year, and for one month prior to hospitalization it had been constantly present. The bleeding was traced to the left kidney, which on removal showed two types of tumour. On its posterior surface, just below the level of the hilus, was a small, rounded, typical hypernephroma. The upper part of the pelvis was filled with " many papillomatous growths with common origin from a rather large pedicle ". This tumour proved on microscopical section to be a papillo-carcinoma showing numerous mitotic figures. In one of the sections tumour cells were seen to have invaded the medullary portion of the kidney. Sections of the growth near the hilus showed the picture of a typical hypernephroma.

In the second case reported by these authors a papilloma of the pelvis was combined with a small (4 mm. × 1 mm.) benign papillary cystadenoma lying just beneath the renal capsule.

Patch and Rhea (1924) reported the following case :—

Male, aged 68. Hæmaturia four months, for which prostatectomy was done in two stages. Bloody urine on leaving the hospital. In the investigation a pyelogram showed the left kidney to be markedly irregular, with broad calices and a filling defect. Nephrectomy, followed three weeks later by ureterectomy. Recurrences in the bladder were treated on many occasions during the next two years. The kidney pelvis contained a papilloma which distended the lower two-thirds and extended into the calices and down the ureter. The pedicle was very small. Histology : A papilloma of low-grade malignancy. A small tumour was present in the cortex, 2·5 × 2 cm., and not approaching the pelvis more nearly than 2 cm. It was for the most part surrounded by a firm connective tissue, but in some parts the tumour cells were in close relationship with the kidney tubules. " The cells generally occur in large and small masses without any pronounced architectural arrangement. There are places, however, where they have a papillary character. Some cells are cystic. Mitotic figures are present but not abundant." Diagnosis, papillary adenocystoma of the kidney of a comparatively low degree of malignancy.

The relationship of these two tumours to each other is discussed. A meticulous search for a connection between the two was made by means of serial sections, but none could be found. The writers think that the papillary material may have been transferred down the tubules to the pelvis, and in support of this point out that the cortical tumour is not completely encapsulated. They are inclined to adopt this view. They also discuss the possibility that the cortical tumour may be a metastasis from the pelvic growth or that each is a metastasis from a remote neoplasm. " The existence of two primaries has," the writers state, " much probability in its favour and cannot be easily controverted."

Professor Wildbolz (1933) described a kidney containing a pelvic papilloma in one part of which numerous mitoses were found and also epithelial cell-nests invading the pelvic wall. A " hypernephroma " of the upper pole was associated with this pelvic tumour.

Balch (1935) has recorded a similar case, a hypernephroma and a papillary carcinoma growing in the same kidney of a man aged 63, the hypernephroma being small (3 cm. in diameter) and subcapsular, as in my patient, and the pelvic growth in the lower lobe. The single symptom, hæmaturia, was referable to the papillary tumour, as in my case, and not to the hypernephroma.

De Vries (1930) published the case of a 59-years old man with hæmaturia. Radiograph and pyelogram showed an oval stone in a horseshoe kidney. Operation : heminephrectomy. A hypernephroma 0·4 cm. in diameter, was present in the lower pole and the pelvis was " thrown into irregular papillomatous folds ".

Melicow (1945), discussing " tumours of the urinary drainage tract ", gives in table form details of some patients. Case No. 13 records a male, aged 65, who was nephrectomized. The kidney contained a " Pap. epithelioma of pelvis Grade II. Clear cell c. of kidney. Vesical papilloma removed 14 yrs. prior to present illness." No further elaboration, case history, or results.

In 1942 Dick reported a " papilloma of the renal pelvis associated with an early renal cell carcinoma ". This paper has not been examined by the author.

Cases have been reported in which an adenocarcinoma (hypernephroma) has been associated with a sarcoma by M. M. Bracken (1936), Rudolf Chwalla (1936), and W. Weisel and M. B. Dockerty (1942).

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PAPILLOMA OF THE RENAL PELVIS IN DYE WORKERS

TWO CASES, ONE OF WHICH SHOWS BILATERAL GROWTHS

By JAS. B. MACALPINE, Manchester

That papillomatous disease of the bladder is more prevalent amongst dye workers than amongst members of the general population has been known since Rehn in 1895 first drew attention to this fact. Of vesical growths the writer has seen many examples referred to him by two dye works in Manchester.

The two patients now reported first attended the urological department of the Salford Royal Hospital with papillomatous disease of the bladder and at a later time developed renal pelvic papillomata. In the second of these patients the papillomata were bilateral. It is of interest that in each of these patients the routine examination of the urine at the dye works first drew attention to the presence of red blood-cells in the urine and was followed by an investigation which revealed papillomatous disease in the bladder. Neither patient had himself observed blood or any symptom of vesical disorder. The renal growths were discovered in one case four years, in the other over five years, after the vesical neoplasm first showed itself.

CASE REPORTS

Case 1.—J. A. B., aged 37.

First seen March 9, 1939. Report from Dr. Scott, Medical Officer to the Chemical Works: "Has worked as process man in manufacture of benzidine and tolidine, carrying out reduction to hydrazo-benzol and hydrazotoluol and subsequent conversion to benzidine and tolidine and their sulphates, from 1927 to date.

"Products handled additional to hydrochlorides and sulphates of above products: Azobenzole occasionally, nitrobenzol, orthonitrotoluol, zinc dust, caustic soda liquor and small amounts powder, paraffin, hydrochloric acid, sodium sulphate.

"So far has noticed nothing wrong with himself. Examined at works at least every three months. Microscopic examination last week showed a large number of red blood-cells in the urine."

Micturition: No trouble. Frequency: Day, hourly (drinks a lot); night, 3–4. Has always passed urine very frequently. No soreness.

Hæmaturia: Patient has never noticed it himself.

General health: Good. Appetite good. No indigestion. Bowels regular. Weight steady.

Previous medical history: No serious illnesses.

On Examination.—Healthy-looking man. Teeth, pyorrhœa. Abdomen, N.A.D. Small sebaceous cyst to right of umbilicus. P.R., N.A.D.

X-ray examination: Renal outlines normal in size and position. Calcified glands over right sacro-iliac joint. Two phleboliths in pelvis.

Excretion urogram: Normal.

Blood-urea, 38 mg. per cent.

Cystoscopy: Urine slight reddish haze. Bladder held 200 c.c. There is a papilloma about $\frac{1}{2}$–$\frac{3}{4}$ in. in diameter in the vault of the bladder. A frothy air bubble had formed around it and this made it difficult to see its exact outline. It seemed fairly well pedunculated and stood out well from the bladder wall. The surface was red, not necrotic, and coarsely nodular. No true fronds. A small daughter papilloma was situated on the left wall of the bladder close to the urethral margin. Stands out well from bladder wall. Coarse fronds. No necrosis.

Urine: R.B.C.'s +. Few E.C.'s, and occasional P.C. seen. No casts. No T.B. Sterile.

April 18: Spinal anæsthetic. Papillomatous areas treated by diathermy. Lavage with silver nitrate. For review in five weeks.

Cystoscopy (June 6): Local anæsthetic. Urine clear. No sign of papillomata in bladder. Review in three months.

Urine: No R.B.C.'s. Pus cells 4/F. A few E.C.'s. No casts. No T.B. Sterile.

Cystoscopy (Nov. 3): Local anæsthetic. Urine crystal clear. Capacity high. No evidence of any recurrence. Mucous membrane normal throughout, apart from a slight hyperæmic area above and to the right of the right ureter. Review in three months.

Cystoscopy (Feb. 13, 1940): Bladder urine clear. There is a reddened area of mucosa in the vault, but no sign of a papilloma. Rest of mucosa normal. Review in three months.

Cystoscopy (May 10): Reddened, congested area in the vault persists, but there is no sign of tumour. Review in three months.

Cystoscopy (July 29): Appearances the same as in previous examination. No sign of tumour. Review in four months.

Cystoscopy (Dec. 16): No sign of papillomata. Review in six months.

Cystoscopy (June 27, 1941): No sign of papillomata. Review in six months.

Cystoscopy (Dec. 8): No sign of papillomata. Review in six months.

Cystoscopy (June 8, 1942): No sign of papillomata. Review in twelve months.

Nov. 13: Complains of difficulty in micturition. No hæmaturia.

Cystoscopy: A papillomatous mass is present just inside the internal meatus from 6–9 o'clock. Nature appears simple. Perurethral diathermy.

Cystoscopy (Feb. 1, 1943): Perurethral diathermy to papillomata at neck of bladder. Review in two months.

Cystoscopy (March 19): The growth is larger than last time and is gaining on us. Swelling noted in left renal area. Large mass palpable, moves on respiration.

Excretion urogram: "Outline of the right renal pelvis and caliceal system is within normal limits. No kidney shadow seen on left side."

Operation (April 16).—Spinal anæsthetic. Kidney enormous—incision extended and portion of last rib resected. Pedicle difficult to isolate—bleeding profuse. Ureter enormously enlarged—divided and found to be filled with growth. Distal end diathermized. Kidney removed (*Fig.* 146).

April 29: Excellent recovery from operation.

Operation (May 7).—Removal of left ureter. Spinal anæsthetic. Iliac approach. Ureter defined, thickened and hard. Isolated with some difficulty. Lower end divided at bladder. Diathermy to entrance into bladder. Some bleeding at upper extremity and ? escape of papillomatous material—not much and very carefully cleaned up.

May 9: Quite good condition. Some bleeding from wound.

May 12: Blood-picture:—

Hb 84 per cent.
M.D. 7·2μ.
R.B.C.'s 4,090,000. C.I. 1·0.

Some red cells are a little hypochromic.

Blood group, II.

June 2: Discharged. Very well. To return in two months. Consider deep X-ray therapy.

Sept. 25: Re-admitted. Reports some hæmaturia. Vesical papilloma diathermized.

FIG. 146.—*Case* 1. The removed kidney is of large size and the cut surface shows the pelvis and the upper third of the much dilated ureter packed with a papilliferous growth. With the exception of a small area near the middle of the organ, the parenchyma is completely replaced by neoplasm, which lies in large loculi separated from each other by fibrous septa. The ureter shows a tendency to stricture formation at one point. The growth of the ureter appears to be a direct extension from that in the pelvis rather than a seediing. Below the point illustrated no growth was discovered.

Cysto-urethroscopy (Sept. 27): Papillomata seen at neck of bladder, but hæmorrhage too severe to fulgurize. Papillomata extremely active.

Cystoscopy (Oct. 1): Spinal anæsthetic. Again too much bleeding after thorough lavage to treat effectively. Hb 80 per cent. Boil of face. Much œdema of right cheek and eye.

Suprapubic diathermy (Oct. 6): Spinal anæsthetic. Large papilloma, right bladder wall, 3 in. × 2 in., pedicle, size of sixpence, apparently is not infiltrating. No secondary tumours. Surface diathermized. Tumour diathermized and removed with electric knife. Large vessels in pedicle diathermized.

Severe reactionary hæmorrhage. Died suddenly. No P.M. permit.

Case 2.—Geo. F., aged 47. Has worked as process man in manufacture of benzidine and tolidine, carrying out reduction to hydrazo-benzol and hydrazo-toluol and subsequent conversion to benzidine and tolidine as their sulphates, from 1923 to February, 1939.

Products handled additional to hydrochlorides and sulphates of above products: Azobenzol occasionally, nitrobenzol, ortho-nitrotoluol, zinc dust, caustic soda liquor and small amounts powder, paraffin, hydrochloric acid, sodium sulphate.

Oct. 26, 1938 (first seen by author): Report sent by doctor of aniline dye works (Dr. Scott): "Has worked for 16 years at —— Aniline Works. A month ago the test at the works was +++ for blood and again last Tuesday week the test showed +++. He works with benzidine."

No frequency or dysuria. Patient himself has not noticed any hæmaturia at all. Appetite good. Bowels normal. General condition satisfactory.

Urine: Neutral, S.G. 1010. Alb. nil. Sugar nil. Urine pus cells, a few. A few R.B.C.'s and E.C.'s. No casts seen. No T.B. seen. Sterile.

Cystoscopy (Nov. 1): Urine almost clear. Bladder held 200 c.c. L.U.O. appeared a little rugose but not abnormal. Small papilloma on lateral wall just inside urethral margin. Size of a small pea. Appeared benign. No induration of base. No sign of daughter papillomata. Complete destruction with diathermy. Silver nitrate. Review in two months.

Excretion urogram: Both kidneys function well and show normal pyelographic contours.

Cystoscopy (Feb. 10, 1939): Small area, about ½ in. in diameter or less, just above and medial to L.U.O., where the mucosa appears as if it was covered with a very delicate mycelium. The fronds appear to arise from many sites, rather like blades of grass out of the ground. No necrosis. Remainder of bladder appears clear. Complete destruction with diathermy. Silver nitrate. Review in two months.

Urine withdrawn at cystoscopy. A few R.B.C.'s and E.C.'s. One or two P.C.'s No casts. No T.B. Sterile.

Cystoscopy (Jan. 3, 1940): Very small papilloma below L.U.O. Destroyed by diathermy. Silver nitrate.

Cystoscopy (May 1): Small 'mossy' area of mucosa on inter-ureteric bar, rather towards the left side. Touched with diathermy.

Cystoscopy (Aug. 2): Small area on inter-ureteric bar denuded of epithelium with small amount of adherent deposit. Does not look neoplastic at the moment.

Cystoscopy (Nov. 11): No sign of papilloma. Review in six months.

Feb. 20, 1941: Complains of pain in crutch. Frequency: day, 2-hourly; night, 0. No hæmaturia. Stream good force and volume.

Urine: First glass, clear; Second glass, clear. Pot. cit. and hyoscyamus.

Cystoscopy (May 12): No sign of papillomata.

Cystoscopy (Nov. 7): No sign of papilloma. Completely symptom-free.

March 26, 1942: Had attack of hæmaturia last week.

Cystoscopy (April 13): No sign of papillomata. Indigo-carmine: R.U.O., 5 min.; L.U.O., 4 min., good. Review in six months..

Sept. 14: Referred by Dr. Scott, who found R.B.C.'s.

Cystoscopy: Urine clear. Capacity normal. Mucosa shows small patchy areas of cystitis but no papillomata anywhere.

Excretion urogram: Normal function. Normal shape.

Blood-urea, 45 mg. per cent.

Cystoscopy (Jan. 15, 1943): Clear.

Feb. 11: Radical cure, R.I.H. (Mr. Wyse). Blood-good repair.

Cystoscopy (July 2): Bladder clear.

Jan. 31, 1944: Complained of hæmaturia.
Cystoscopy (local): Bladder healthy. No neoplasm.
Excretion urogram: ? Renal papillomata. Large right kidney not functioning. Left kidney, pelvic defect at base of upper calix. This defect is constant on all films, and repeat films taken on another day showed precisely the same defect. It is regarded as evidence of a pelvic papilloma of the left kidney (*Fig.* 147).

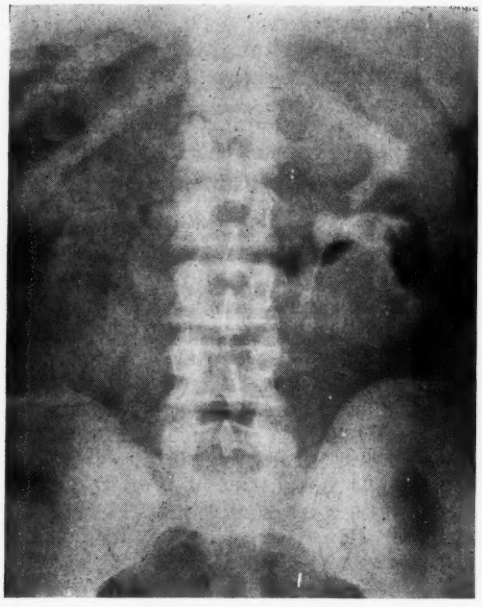

FIG. 147.—Excretion urogram. Right kidney not functioning; left kidney pelvis defect at base of upper calix, accurately portraying the lesion seen in accompanying coloured drawing, *Fig.* 148.

Blood-urea, 60 mg. per cent.
May 23: Admitted with anuria of 24-hours' duration.
Examination: Very sick. Huge palpable right kidney. Left kidney not felt.
Cystoscopy: No urine in bladder. Right ureter catheterized—no urine. Left ureter catheterized—no urine. Left ureteric catheter left in situ. Sulphates, etc.
May 24: Has drained about 30 oz. Catheter in ureter removed.

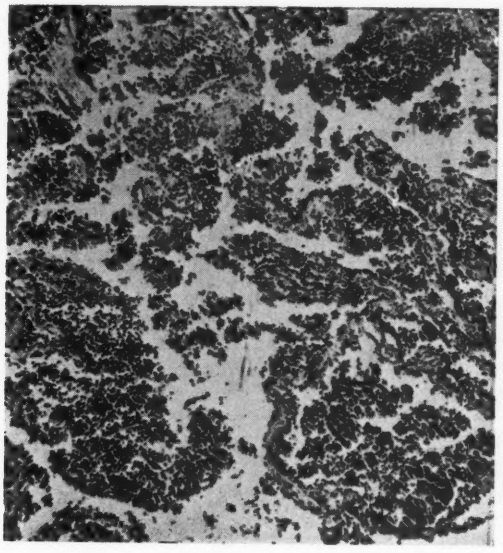

FIG. 149.—Section showing villous papillo-carcinoma.

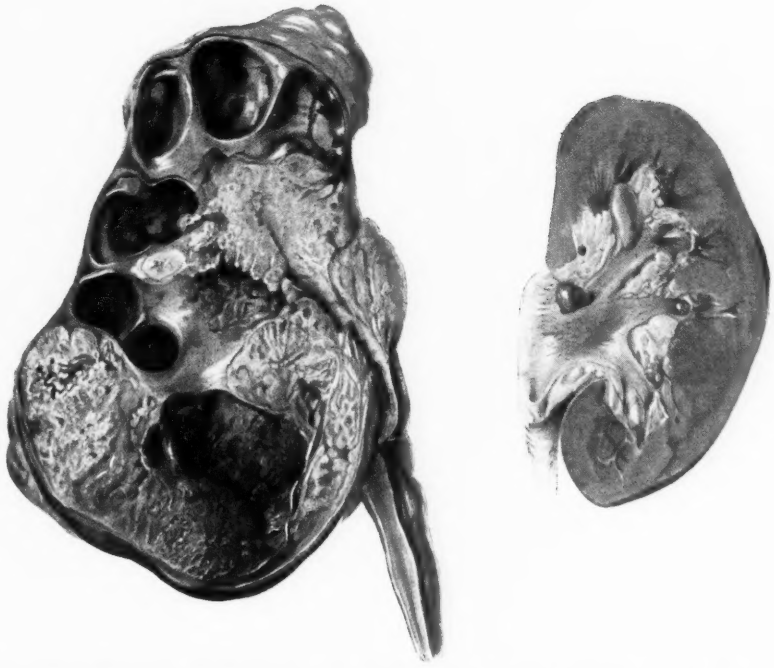

FIG. 148.—Bilateral renal papillomata. On the right side the organ is greatly enlarged (3½ lb.). The whole of the pelvis is filled with papillomatous growth and the ureteropelvic outlet is occluded, a bristle passing with difficulty from below into the pelvis. New growth has replaced the parenchyma of the lower pole and approaches the middle and upper sections of the gland, which for the most part show severe hydronephrotic changes. No healthy renal tissue can be detected. The left kidney is but slightly increased in size and the parenchyma is well preserved. A single, rounded, sessile or subsessile papilloma occupies the point of junction of the upper major calix with the pelvis proper, and this calix shows moderate dilatation. Cf. *Fig.* 147.

May 25 : Recurrence of anuria with severe sickness.
May 29 : Death from uræmia.
May 30 : Post-mortem examination : Huge papillo-carcinoma of right kidney. Weight, 3¼ lb. Left kidney : cortex atrophied. Papilloma at base of upper calix, causing some obstruction of this calix. Ureters both healthy. Bladder clear (*Fig.* 148).

Pathological Report.—Villous papilloma (*Fig.* 149). Malignancy not pronounced.

DISCUSSION

In each case, though excretion urograms had been obtained at the time of the original investigation and on at least one subsequent occasion, the neoplasm was regrettably overlooked till it had grown to a large size, in spite of the fact that the bladders had been under periodic cystoscopic review. In justification of this failure of observation, it may be pointed out that after the bladder had been cleared of papillomata a prolonged period elapsed—in one instance more than three years, and in the other from January, 1940, till his death in May, 1944—during which the bladder remained free from papillomata and the patient virtually free from symptoms. The preceding vesical disease had focused attention unduly on that organ. Subsequently it became routine practice to order excretion urograms at relatively short intervals for these papilloma-forming subjects.

In the first patient, having regard to the long time in which bladder growths were in abeyance and symptoms were absent, the kidney tumour must be regarded as an independent primary. The author also regards the tumours of the second patient as three primaries, and, if this view is correct, the presence of three such primaries denotes the strength of the stimulant, whatever that may prove to be, to umour formation.

The question whether we should ever encounter papillomatous disease of the upper urinary tree in a dye worker had often been mooted, but these were the first and only examples seen at the clinic.

A search of the literature has shown that 6 other examples of pelvic papillomata in dye workers have been recorded, by Rehn (1905), Leuenberger (1912), Nassauer (1919-20), Sebening (1930), Mueller (1936), and Gay (1937). It is of interest that in Sebening's patient, who had been for 30 years in a dye works, the tumour occurred in a hydronephrosis and in Mueller's in the upper part of a double kidney. In health the urine passes quickly through the pelvis and ureter and there is but little time in which any contained carcinogenic agents can act. The inadequate drainage of a hydronephrosis or a malformed kidney, resulting, as it presumably does, in prolonged contact with the harmful substance, may predispose to the development of a tumour. Mueller (1940) has also reported a case in which a tumour occurred in the ureter of a man of 42, who from the age of 18 to 26 worked in benzidine but had had no further contacts with dangerous substances since that time.

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THE TREATMENT OF BLADDER CANCER

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ALTHOUGH symptoms of bladder disease were known to the ancients, it is really only during the past sixty years that advances have been made in the diagnosis, pathological interpretation, and treatment of bladder cancers : and even now the problem of what is the safest and best treatment is still absorbing, and is not yet settled. It is the purpose of this paper to point out some of the disappointments and disillusions that have been associated with the attempts to eradicate the disease : and our results are a corrective of complacency.

Approaching the subject from the historical aspect it is interesting to note that in the aphorisms ascribed to Hippocrates, hæmaturia, pyuria, strangury, and hypogastric and perineal pain are all recorded ; but, familiar as were the Hippocratic writers with cancer of the superficial organs, there is no evidence that they associated these symptoms with malignant disease in the bladder.

Likewise, the dwellers in the Nile Valley possibly saw examples of cancer of the bladder associated with bilharzia ; but since there is no written word to quote, it can only be surmised either that the records have been lost or, more likely, that the significance of the condition passed unrecognized. In fact, it was not until the time of Ambrose Paré (1510–90), who noted axillary swellings in cases of breast cancer, that one peculiar quality of malignant disease was appreciated : and it was for another French surgeon, François Le Dran (1685–1770) to associate the tendency of cancer to recur locally in spite of careful operation.

The first recorded clear description of a cancer of the bladder was made by a Dutchman, Nicolaas Tulp (1593)—the central figure in Rembrandt's " School of Anatomy ". Tulp carried out a post-mortem examination on a patient who had suffered from a recto-vesical fistula, and confirmed the diagnosis of cancer.

Operations for bladder tumours have been performed at least since the early part of the seventeenth century, and Albarran has ascribed the first recorded operation to Covillard, of Montelimard, in the south of France. Covillard recorded his operation in his *Observationes Iatio-chirugiques* (1639), and wrote that while operating for stone through a lateral perineal approach, he recognized a tumour which he " grasped with his forceps and it came away in a few day's time ".

Naturally, the development of lithotomy for bladder stones in the seventeenth and eighteenth

centuries encouraged the recognition of bladder tumours; but as late as 1747, Warner, an Edinburgh graduate who came south and joined the staff of Guy's Hospital and became Master of the Surgeons' Company—the forerunner of the Royal College of Surgeons—wrote, after removing a pedunculated tumour of the bladder through the urethra of a female patient, "I believe that hitherto no one has attempted the cure of this disorder by extirpation, nor indeed can it be supposed that the instances are frequent where the operation is practicable". As we know now, his attempt was preceded by that of Covillard, but his statement emphasizes the rarity of the operation at that time; and although the operation through the urethra and perineum was to be repeated, it was not until the latter half of the nineteenth century that Billroth, of Vienna, carried out a planned suprapubic approach for a bladder growth. In 1874 Billroth, operating for a tumour of the bladder, found that the mass was too large to be removed through the perineal exposure and proceeded straight away to a suprapubic resection. But even Billroth made no attempt to excise the full thickness of the bladder wall with the growth; it was not until the impetus given to the understanding of morbid processes by the great European pathologists—especially by Virchow's conception of cellular pathology—that it was realized that more than a local removal of a growth was necessary. However, by the end of the century Albarran (1891), working in Guyon's clinic in Paris, was able to quote twenty cases of bladder cancer treated by suprapubic resection.

But, as has been the case in the treatment of malignant disease elsewhere in the body, the early attempts were not radical enough to extirpate the disease, and it is not difficult for us now to understand that recurrence was bound to be the usual result.

The adoption of the Trendelenburg position (1881) and the operation by Sonnenburg (1885), who carried out a partial cystectomy with excision of the local peritoneum, marked further steps forward; but it was not until the discovery and the practical application of the cystoscope by Nitze (1887) that a wider conception of the problem could really begin to be appreciated and developed. Nitze elaborated the method of transurethral operation and treated over a hundred cases by engaging the bladder tumours in a snare on the end of the telescope, and afterwards cauterizing the raw base of the tumour.

The results of Nitze's work helped to make some clinical distinction between benign and malignant growths, and in fact he specifically advised against snaring any but benign tumours. He also noted the so-called benign recurrences in follow-up examinations, and pointed out that they might appear in the bladder at places remote from the site of the primary growth.

A further advance, a few years before the first World War, was Edwin Beer's use of the high-frequency current for transurethral diathermy; while at about the same time radium applications in one form or another were introduced and developed by Hugh Young (1923), of Baltimore, and Barringer (1922), of New York.

As surgical technique improved, even more radical surgery became possible, and although total cystectomy had been carried out by Bardenheuer as early as 1887, it was not until 1915 that the French surgeons advocated this as the method of choice for the treatment of cancer of the bladder. Bardenheuer's patient survived only a few days because the cut ends of the ureters were left to drain into the peritoneal cavity, but as early as 1895 Wassiljew had carried out cystectomy and cutaneous ureterostomy, and by the end of the first decade of this present century the problem of deviation of the urine had been intensively studied, and by 1915 Edwin Beer had advocated and carried out cutaneous ureterostomies as a routine step in the radical treatment of cancer of the bladder.

The first successful transplantation of the ureters to the bowel has been ascribed to John Simon (1852)—afterwards Sir John Simon—of St. Thomas's Hospital. Simon, who ultimately deserted surgery and became a famous sanitarian, described in the medical press of his time an operation for ectopia of the bladder which he carried out in 1852. This patient lived twelve months after transplantation of the ureters into the rectum, voiding urine from the bowel. In 1891, Kuester actually succeeded in carrying out a complete cystectomy with transplantation of the ureters into the rectum in a case of cancer of the bladder, and his patient survived for five days before dying from peritonitis and a renal infection—especially interesting to us now because, as will be shown, the same two complications are as malign and fatal to this very day.

By the end of the nineteenth century, several successful ureteric transplantations had been done, but the majority were for congenital abnormalities such as ectopia of the bladder; and Peterson, in an excellent and comprehensive review of the subject in 1900, was able to quote only 6 cases of ureteric transplantation for cancer of the bladder. Various techniques were introduced, including transplantation of a cuff of the bladder with the ureters (Maydl, 1894), and an extraperitoneal method of ureteric transplantation (Peters, 1901).

During the first decades of the twentieth century attempts to master the technique of ureteric transplantation were made in these islands by Harold Stiles, of Edinburgh, and Grey Turner, of Newcastle and the British Post-graduate Medical School, London. But again the anastomoses were done chiefly for congenital abnormalities of the lower urinary tract, and in spite of Coffey's work in the United States in the time between the two World Wars, Grey Turner was of the opinion that the operation of ureterocolic transplantation for malignant disease of the bladder must still be considered pioneer surgery, and that a high mortality was to be expected even in experienced hands.

In 1931 Coffey reported his series of transplantation of the ureters in 35 patients, and his results were certainly encouraging. Sixteen of the patients had suffered from malignant disease of the bladder, and of these only 4 (25 per cent) had died of the operation. Yet Coffey's late results were somewhat disappointing, as a critical analysis shows.

Of the 16 patients who suffered from malignant disease of the bladder, 4 died of the operation and

5 others within seventeen months. Alternatively, his series shows that 25 per cent died of the operation (2 patients after total cystectomy and bilateral ureteric transplantation at one stage, and 2 after bilateral ureteric transplantation at one stage), and a further 25 per cent died within a year: i.e. 50 per cent were dead within a year because of, or in spite of, apparently radical surgery (*Table I*).

Table I.—Results of Ureterocolic Anastomosis and Cystectomy for Cancer of the Bladder (Coffey, 1931)

Total cases: 16		
Operative deaths	4	
Later deaths	5	1 died 2 months after operation 1 died 6 months after operation 1 died 10 months after operation 1 died 11 months after operation 1 died 17 months after operation
Too soon to prognose	1	
Patients alive	6	1 alive 12 months 1 alive 14 months (papilloma) 1 alive 17 months 2 alive 24 months 1 alive 38 months
Operative mortality		25 per cent
Mortality within one year		25 per cent

Furthermore, not every case of cancer of the bladder coming to hospital is suitable for partial or complete cystectomy with ureteric transplantation, as is shown by a review of the patients presenting at the British Post-graduate Medical School, Hammersmith Hospital, during the years 1935–46.

In this period the total number of patients who suffered from carcinoma of the bladder was 76; 21 of these (28 per cent) were considered to have a chance of cure by complete cystectomy, and 9 (12 per cent) were regarded as being suitable for partial cystectomy. Of the remainder, 3 ceased to attend hospital, 16 refused or were not advised to undergo any form of surgical treatment, and 27 were submitted to a palliative or a diagnostic procedure. The operations performed in this last group were: bilateral cutaneous ureterostomy 1, suprapubic cystostomy 16, suprapubic cystostomy with diathermy 6, suprapubic cystostomy with deep X rays 2, transurethral fulguration 1, biopsy of gland of neck 1. The last patient presented with multiple lymph-node swellings and without urinary symptoms. (*Table II.*)

Table II.—British Post-graduate Medical School Series of Cancer of the Bladder (1935–46)

Total cases: 76	
Only one attendance at hospital	3
Surgical treatment refused or not advised	16
Suitable for palliative treatment only	27
Suitable for radical treatment*	30

* By radical treatment is meant either partial cystectomy or complete cystectomy after ureterocolic anastomosis.

ANALYSIS OF TREATMENT AND COMMENTARY

1. Ureteric Transplantation and Complete Cystectomy.—Of 21 patients in whom a complete cystectomy and ureteric transplantation was contemplated, 12 died at some stage of the operative programme. Eight died after bilateral ureteric transplantation, 1 died after right ureteric transplantation and left nephrectomy, and 3 died after the bladder excision.

The cause of death in these cases was as follows:—

a. Bilateral Ureteric Transplantation: Peritonitis and pulmonary embolism 1, peritonitis and ileus 1, pelvic peritonitis and atrophy of the heart 1, pulmonary embolism 1, pelvic peritonitis 1, peritonitis and pulmonary embolism 1, bronchopneumonia and pyelonephritis 1, pneumonia and uræmia 1.

b. Right Ureteric Transplantation and Left Nephrectomy: Bronchiolitis and pulmonary œdema 1.

c. Bladder Excision: Bronchopneumonia and rheumatic carditis 1, pelvic peritonitis and ileus 1, peritonitis 1. (*Table III.*)

Table III.—British Post-graduate Medical School Series of Cancer of the Bladder. Operative Mortality of Ureterocolic Anastomosis and Complete Cystectomy

Total cases: 21		
Operative deaths: 12		
After bilateral ureteric transplantation:—		
Peritonitis: pulmonary embolism	1	8
Peritonitis: ileus	1	
Pelvic peritonitis: atrophy of heart	1	
Pulmonary embolism	1	
Pelvic peritonitis	1	
Peritonitis: pulmonary embolism	1	
Bronchopneumonia: pyelonephritis	1	
Pneumonia and uræmia	1	
After right ureteric transplantation and left nephrectomy:—		
Bronchiolitis and pulmonary œdema	1	1
After bladder excision:—		
Bronchopneumonia: rheumatic carditis	1	3
Pelvic peritonitis: ileus	1	
Peritonitis	1	
	Total	12
Total operative mortality	57 per cent	

Thus in our series there is an operative mortality of 57 per cent, which is comparable with that of 56 per cent presented by Hinman and Smith (1939) and with that of 64 per cent by Walker Taylor (1931). I have been unable to find the causes of death in the fatal cases in Hinman and Smith's series, but in that of Walker Taylor 4 out of the 14 cases had a peritoneal infection, while 2 died on the third day of "asthenia" and there was no post-mortem. In our own series, infection of the peritoneal cavity occurred in no less than 7 out of the 12 fatal cases. (*Table IV.*)

Table IV.—Other Authors' Series: Operative Mortality of Ureterocolic Anastomosis and Complete Cystectomy

Hinman and Smith (1939)		*Walker-Taylor* (1931)	
Total cases	50	Total cases	14
Deaths	28 (56 per cent)	Deaths	9 (64 per cent)
		Peritoneal infection	4
		Died on third day; asthenia; no post-mortem	2
		Not recorded	3

2. Partial Cystectomy.—Although partial cystectomy is obviously a less severe procedure than complete cystectomy, it can be employed only if the growth is favourably placed. If it is at the fundus or on the anterior wall, local excision may be adequate, while if the tumour involves one ureter, a local excision of the tumour and adjacent bladder, together with division and reimplantation of the ureter into the bladder, may be the method of choice. But an analysis of the sites of the tumours in our series shows that this more fortunate state of affairs is not common and of 71 cases analysed only 12

could be considered suitable for treatment by partial cystectomy (*Fig.* 150).

Jewett (1944) has stated that tumours growing at sites which might be thought to be most suitable for

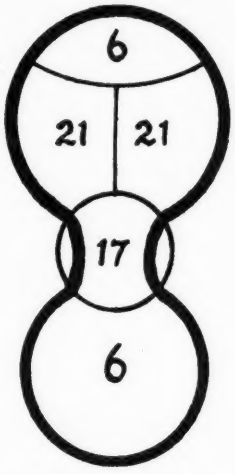

FIG. 150.—Sites of bladder cancers (71 cases). (British Post-graduate Medical School series, 1935–46.)

treatment by partial cystectomy have a higher incidence of metastases than those situated on the posterior wall of the bladder, possibly because of the shorter course of the lymphatics before they leave the bladder. Further, he advises that a margin of 4 cm. around the growth is necessary for safety. This, however, leaves a very small bladder, and uncomfortable frequency of micturition is a likely result.

Failure of adequate partial cystectomy dooms the patient to recurrence, which was observed in 5 out of the 9 cases so treated in our series. (*Table V.*)

Table V.—BRITISH POST-GRADUATE MEDICAL SCHOOL SERIES: PARTIAL CYSTECTOMY

Total cases: 9	
Operative mortality	Nil
Recurrence of bladder growth	5

3. Cutaneous Ureterostomy.—Experience of this operation in the present series is limited to one patient who died from peritonitis and uræmia four days after bilateral cutaneous ureterostomy.

I myself looked after this patient and speak from personal experience when I say that the management of the ureteric catheters is not easy and their replacement if they come adrift is, to say the least of it, not a simple procedure. Ewart and Dick, writing from the Lahey clinic in 1941, hold a similar opinion, and reserve cutaneous ureterostomy for exceptional cases. I recently considered this operation indicated, for example, in an elderly female who suffered from carcinoma of the bladder around the internal urinary meatus, and from a carcinoma of the rectum as well, both quite separate and distinct tumours.

LATE RESULTS OF TREATMENT

1. Complete Cystectomy and Ureterocolic Transplantation.—The late results of our cases bear a close resemblance to those of Coffey's 1931 series. Of 9 patients successfully emerging from the total cystectomy and ureteric transplantation, 1 died twelve months after discharge from hospital, and at post-mortem no recurrence was found; 3 died of their disease within two and a quarter years from the time when they were first seen; and of the other patients 1 is too recent to assess the eventual prognosis, 1 is alive and well six months after operation, 1 is alive and well twenty-one months after operation, 1 is alive and well after two years, while in the only 1 long-term survival, four years, the condition was probably a papilliferous growth and had been treated elsewhere on more than one occasion by suprapubic fulguration and by interstitial radon seeds; when the histological report was received after total cystectomy, it stated that no growth could be found in a grossly contracted bladder. (*Table VI.*)

Table VI.—BRITISH POST-GRADUATE MEDICAL SCHOOL SERIES. LATE RESULTS OF URETERIC TRANSPLANTATION AND COMPLETE CYSTECTOMY

Cases: 9

1 died	5 months (Metastases left groin)
1 died	12 months (Bronchopneumonia: no recurrence)
1 died	20 months (Metastases left trochanter)
1 died	29 months (Metastases left flank, right femur, and pelvis)
1 well	3 months (Too soon to assess)
1 well	6 months
1 well	21 months
1 well	24 months (Villous papilloma of borderline character)
1 well	48 months (Old papilloma with contracted bladder)

2. Partial Cystectomy.—Of 9 patients in our series treated by partial cystectomy, 5 developed recurrences at intervals varying from three months to four and a half years, and of these, 3 died shortly after the recurrence was noted: 1 of the nine attended for only a month and 1 for only eight months after discharge from hospital: only 2 appear to be controlled —1 at twenty months and 1 at thirty-two months after operation. These last two patients still run the risk, for one of the patients who died did not develop the fatal recurrence until four and a half years after local excision. (*Table VII.*)

Table VII.—BRITISH POST-GRADUATE MEDICAL SCHOOL SERIES. LATE RESULTS OF PARTIAL CYSTECTOMY

Total cases: 9

Recurrences	5
1 at 3 months:	Death after suprapubic fulguration and left ureteric transplantation
1 at 4 months:	Death: metastases para-aortic glands
1 at 10 months:	Not seen again
1 at 32 months:	Death from pneumonia after bilateral ureteric transplantation and complete cystectomy
1 at 54 months:	Death: metastases liver and lungs: bilateral renal infection
Survivals	4
1 well	1 month (not seen again)
1 well	8 months (not seen again)
1 well	20 months (not seen again)
1 well	32 months (not seen again)

3. Results in Complete Series.—If the whole series of 76 cases is considered, including those patients treated palliatively, only 16 were known to have survived for longer than six months from the time when they were first seen at this hospital, while it is known that 44 of the 76 were dead within six months.

The fate of the 16 patients who were not treated by surgery, either because the patients refused or

it was not advised, is shown in the following table, and it will be seen that with two exceptions, who were not fully investigated, the members of this group were not in fact suitable for radical treatment.

a. Operation not advised (10 *patients*) :—

1 Glands both groins and armpits.
1 Glands along left external iliac vessels into loin.
1 General condition very poor. Mass left loin. I.V.P. no secretion left kidney. Blood-urea 38.
1 Admitted with hemiplegia and auricular fibrillation. Died ten days.
1 Uræmia. Retention. Catheter. Died nine days. Metastases in pelvic lymph-glands.
1 Spread to pubic bone and skin. Death after extradural anæsthesia.
1 Right hydronephrosis. No secretion left kidney at sixty minutes.
1 Died seven days. Metastases right regional glands. Fatty and dilated heart. Œdema of lungs.
1 Died day of admission. Left renal calculi. Right hydronephrosis and hydro-ureter. Uræmia.
1 Died two months. General condition very poor. Growth locally very extensive.

b. Refused surgical treatment (6 *patients*) :—

2 Not fully investigated.
1 Re-admitted six months. Died heart disease. No metastases.
1 Re-admitted two months. Left hydronephrosis. No secretion right kidney at sixty minutes. Blood-urea 57.
1 Re-admitted inoperable. General inanition. Uræmia. Metastases.
1 Re-admitted four months. Died one month later. Metastases, regional and aortic lymph-nodes, liver, left adrenal, and thoracolumbar vertebræ. Bilateral hydronephrosis and hydro-ureters. Acute hæmorrhagic cystitis.

These findings after analysis remind one of the similar problem of treatment of cancer of the stomach, and it is tempting to look for alternative methods of treatment.

ALTERNATIVE METHODS OF TREATMENT

1. Surgical Modifications : Search for a Safety Factor.—The autopsies of the fatal operations in our series of transplantation of the ureters and complete cystectomy emphasize that peritonitis is a great immediate danger, and it is possible that modifications of the surgical programme would help to overcome this risk. Beer, some thirty years ago, favoured the operation of bilateral cutaneous ureterostomy as the primary stage in the surgical treatment of carcinoma of the bladder, and its value may merit reconsideration. If this first stage is modified to total excision of the bladder, the ureters can be divided at the bladder and brought out extraperitoneally through small counter-incisions in both iliac fossæ. Then, in two or three weeks, when the patient's general condition has improved, ureterocolic and ureterocæcal transplantation can be completed. Nevertheless, primary cutaneous ureterostomy is not a simple procedure and sloughing, leakage, œdema, and blockage of the ureter are all potential hazards.

As long ago as 1905, F. S. Watson, in the United States, advised bilateral nephrostomies as a method of palliation or preparatory to total cystectomy, and I have carried this out recently on one patient (not included in the present series). The two nephrostomies and the bilateral ureterocolic transplant were done at weekly intervals before the final cystectomy was completed.

Alternatively, in a further two patients (not included in the present series) I have defunctioned the distal half of the large bowel as a preliminary operation. Transverse colostomy, with complete division of the bowel and suturing of the proximal cut end of the distal loop, was done and the isolated loop was dropped back into the peritoneal cavity. By so doing, the risk of infection after the ureterocolic transplant is minimized because the organisms in the isolated loop will have no fæcal matter on which to live and will have to fight for survival against sulphasuxadine and penicillin administered by frequent irrigations through the anal canal. This method of treatment is similar to that used by Krönig (1907) some forty years ago, with the exception that my patients do not have a leak of urine through the colostomy because the distal loop of colon is closed. (Professor Grey Turner informs me that Thomas Myles, of Dublin, described a similar method some time ago, but I have been unable to find the recorded account.)

Lastly reference must be made to the principle of the extraperitoneal method of ureteric transplantation first introduced by Peters (1901) and advocated by Riches at the Middlesex Hospital in recent years. If leakage develops from the site of the ureterocolic transplant, provided a drain is used, the risk is minimal if the extravasation and infection is extra- and not intraperitoneal.

In all methods of deviation of the urinary flow used in the treatment of malignant disease of the bladder, the help given by the sulpha drugs and penicillin will be utilized to the full.

2. X rays.—The value of deep X-rays in the treatment of bladder cancer has not yet been fully assessed because the total number of patients referred to the radiotherapist is not large and the group contains a large proportion of late cases. In our own series there is only one outstanding example of a patient who was treated by deep X-rays after marsupialization of the bladder. He survived for three years, to die eventually of metastases in the spine and pyelonephritis. It is notable that at post-mortem there was no evidence of local bladder recurrence.

The consensus of opinion is that X rays are seldom curative but should be used more frequently as a method of palliation. Yet the Holt Radium Institute record (1946), admittedly in a small series, of a 60 per cent five-year survival in the early cases and a 17 per cent five-year survival in the late is as encouraging as our results with surgery. In fairness to surgery, it should be pointed out that the majority of our patients would come into the category of late cases.

Further, it is difficult to assess accurately just how much the patients are upset by irradiation and the degree of bladder irritation they must suffer as the price of possible ' cure '. The morbidity of the X-ray treatment is uncertain.

3. Radium.—Jacobs (1943), of Glasgow, has had a wide experience in the treatment of bladder cancers by interstitial radium, and has reported a series of 93 cases out of which there were 8 operative deaths and 26 deaths subsequently from the disease. His operative mortality of 9 per cent is to be compared with ours for partial cystectomy and for complete cystectomy with ureteric transplantation—that is, with an operative mortality of 40 per cent. Further, Jacobs was able to report 31 patients alive and tumour-free for periods varying from nine years to

one year, while 15 per cent of his patients were alive for more than three years, as compared with ours of only 6·6 per cent (2 patients out of 30).

These results of interstitial irradiation seem to compare favourably with those achieved by surgery alone, but it is interesting to read in the later part of his paper that Jacobs himself prefers partial cystectomy where possible, though he is able to perform this operation only in about one-third of his patients. (*Table VIII.*)

Table VIII.—Comparison of Results of Surgery and Irradiation for Cancer of the Bladder

	Surgery (B.P.G.M.S.) (1935–46)	X Rays (Holt R.I., 1947)	Interstitial Radium (Jacobs, 1943)
Operative mortality	40 per cent*	—	9 per cent
3-year survival	6·6 per cent	Early cases 60 per cent Late cases 17 per cent	15 per cent

* Combined figures for partial cystectomy and complete cystectomy and ureterocolic anastomosis.

WHAT OF THE FUTURE?

As is the case with almost all malignant growths, early diagnosis will, without doubt, help us to increase the prospects of cure. Jewett has computed that if a bladder tumour is confined to the mucous membrane alone (Group *I*), there is a potential curability of 100 per cent; if there is infiltration of the muscularis, but not penetration through it (Group II), there is a potential curability of 86 per cent; whereas if there is perivesical infiltration (Group *III*), the potential curability falls to 26 per cent.

In Jewett's series (collected from autopsies at the Johns Hopkins Hospital during the years 1919–44) Group III was proportionally very large, and in our series, too, this grade of disease unfortunately is still too common.

As would be expected, the incidence of metastases in the late cases is high, and in Jewett's series it was 7 per cent in Group II and 58 per cent in Group III.

In our series, 55 cases were analysed and metastases were found by clinical and X-ray examination in 6 patients (11 per cent). The sites of these metastases were: para-aortic lymph-glands 1; left external iliac lymph-glands 1; both groins and both armpits 1; left ilium and left part of sacrum 1; left supraclavicular lymph-glands 1; liver 1; while in a further 14 patients (25 per cent), metastases were found at autopsy as follows:—

1 Lumbar lymph-glands.
1 Lungs; bones; groins.
1 Peri-ureteral.
1 Left acetabulum; inguinal lymph-glands.
1 Lumbar lymph-glands.
1 Pelvic lymph-glands.
1 Neck; armpits; mediastinum; groins.
1 Pelvic lymph-glands.
1 Pancreas; liver; pelvic lymph-glands.
1 Pelvic lymph-glands.
1 Regional and aortic lymph-glands; liver; left adrenal; dorsolumbar vertebræ.
1 Dorsal vertebræ.
1 Liver.
1 Pelvic lymph-glands.

In 16 cases no metastases were found at operation, but in 4 of these they developed later:—

1 Both groins	5 months
1 Both armpits	11 months
1 Right femur; left flank	28 months
1 D. 10 and L. 5 vertebræ	36 months

In 19 cases (34 per cent), however, no metastases were found post mortem; this considerable group should be amenable to radical surgery (*Table IX* and *Fig.* 151).

Table IX.—British Post-graduate Medical School Series. Incidence of Metastases in Cancer of the Bladder

55 cases investigated clinically, at operation, at post-mortem.
6 found clinically and by X rays
16 not found at operation (but 4 developed metastases later):—
1 at 5 months (both groins)
1 at 11 months (both armpits)
1 at 28 months (right femur and left flank)
1 at 36 months (dorsal 10, and lumbar 5 vertebræ)
14 found at post-mortem
19 no metastases found at post-mortem

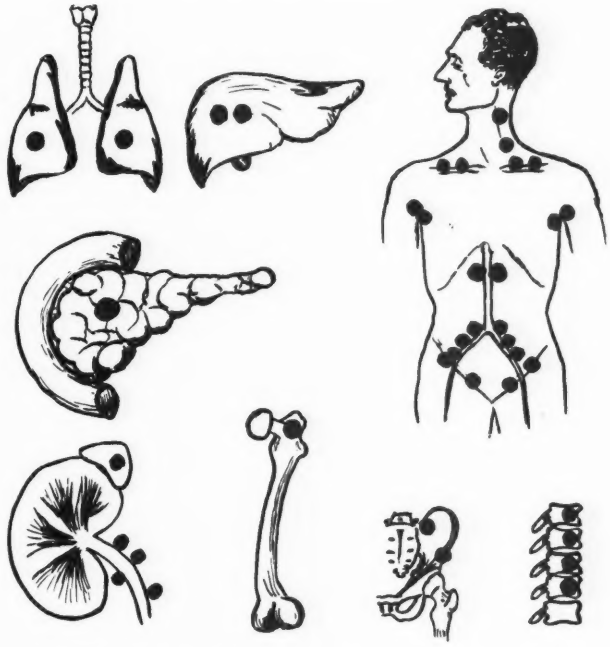

Fig. 151.—Sites of metastases of bladder cancers in the British Post-graduate Medical School series, 1935–46. (This is not intended to show the incidence.)

The other great problem to be overcome is infection of the upper urinary tract from ureteric involvement and obstruction by growth. The more extensive the growth (or the later the patient comes for treatment) the greater is the likelihood of ureteric obstruction; in our series, 62 patients were investigated by excretion urography or at operation, or at post-mortem, and obstruction of one or both ureters was present in 37 (*Table X*).

Table X.—British Post-graduate Medical School Series. Ureteric Obstruction (Excretion Urography, Operation, and Autopsy Findings)

Cases: 62
37 obstruction present
25 no obstruction present

Earlier diagnosis then, must be the first consideration: routine cystoscopy for any urological symptom should be done as soon as possible after its onset, but even this is no safeguard. The frequency must be admitted of so-called benign papillomas which are controlled, apparently successfully, for some time by repeated transurethral fulguration, but which eventually prove to be malignant and need more radical treatment. Careful follow-up control by repeated cystoscopy should enable us to surmise that a recurring tumour is malignant, and with early diagnosis at this stage it would seem that partial cystectomy—only provided that the growth is suitably situated and the operation radical enough—will offer a low operative mortality and a reasonable promise of cure.

What is to be the position of complete cystectomy with ureteric transplantation ? Surely, there can be no doubt theoretically that wide and complete radical excision should offer the best prospects of cure of a malignant process; and even if it be argued that in some cases partial cystectomy can eradicate a tumour as successfully as complete cystectomy, there cannot possibly be a bladder recurrence after complete cystectomy and the patient is at least assured that the bladder symptoms can never recur. At present, the high operative mortality and the not too encouraging late results perhaps question our justification in advising a patient to submit to such a heroic procedure and, having survived it, to have to endure the inconvenience of a cloaca. However, given early cases in a better general condition, and the operation done in stages with a proper use of antibacterial drugs, it should surely be possible to bring the operative mortality and morbidity to something akin to that of operations for cancer of the colon or the lung.

When these favourable conditions become common, and until biophysical research into the treatment of all malignant disease is more fully advanced, even more radical surgery with planned exposure of the lymph-glands along the iliac vessels and their removal, is likely to be part of the routine operation for cancer of the bladder.

In the meantime, before final judgement is pronounced, it is surely our duty to report as accurately and with as much detail as we can, comparable series of cases treated by radical surgery and by radiotherapy, and in time to analyse and assess which is the safest and best method for the patient.

I express my thanks to Emeritus Professor Grey Turner, my former teacher, for introducing me to a subject with which his name will always be associated, for his constructive criticism, and for allowing me access to so much of his material; to Mr. E. W. Riches, M.C., for kindly reading the proofs; and to Sir Allen Daley for permission to publish this paper.

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CARCINOMA OF THE AMPULLA OF VATER*

BY JOHN MORLEY

THE six cases of carcinoma of the ampulla of Vater recorded here were all treated by resection of the whole of the second part of the duodenum along with a considerable portion of the head of the pancreas, the pancreatic duct being tied and not anastomosed with the alimentary tract. The operations were all carried out in two stages, very much as described by Whipple, Parsons, and Mullins in 1935 in the third of the three cases they then reported.

During the four years in which these cases occurred, several patients with carcinoma of the head of the pancreas were explored, but in none of them was a radical removal judged feasible. Carcinoma of the head of the pancreas is definitely more common than ampullary carcinoma, though accurate figures of their relative frequency do not appear to be available.

* A paper read before the Manchester Surgical Society, Feb. 11, 1947.

Diagnosis.—A steadily progressive obstructive jaundice, usually, but not always, unaccompanied by pain, coming on in a patient of cancer age, and associated with a palpable, non-tender enlargement of the gall-bladder, gives a clinical picture that may mean carcinoma of either the head of the pancreas or of the ampulla, and up to this point Courvoisier's so-called 'law' hardly ever lets us down. (Chronic pancreatitis as a cause of the same symptoms is so rare that one has almost come to regard it as a figment of the text-books.) In some cases, however, perhaps as many as 50 per cent, the enlargement of the liver is so great as to cover the distended gall-bladder and make it impossible to palpate.

Another occasional diagnostic difficulty arises where gall-stones are impacted both in the common duct and in the cystic duct or the neck of the gall-bladder. In this rare combination we find also jaundice associated with a palpably distended gall-bladder, but there is always a history of biliary colic and of tenderness over the gall-bladder during the acute stage of obstructive cholecystitis which precedes the formation of a mucocele.

The differential diagnosis between carcinoma of the head of the pancreas and ampullary carcinoma is seldom possible before the abdomen is explored. In some few cases the radiologist may outline a fungating ampullary neoplasm as a filling defect on the medial aspect of the second part of the duodemun, or may suspect a massive carcinoma of the head of the pancreas because of a widening of the duodenal circle. In none of my cases have these refinements of radiological diagnosis given us a precise pre-operative diagnosis.

FIG. 152.—A, First stage: Cholecystogastrostomy and Gastrojejunostomy. B, Resection of second part of duodenum and pancreas with growth. C, Condition at completion of operation.

CASE REPORTS

Case 1.—A man, aged 42, gave a history of gradually deepening jaundice for three and a half months. During this period he had felt ill and had lost flesh. There had been no pain.

Previous Health.—There was a history of flatulence and occasional vomiting over the past twenty years, but no pain.

ON ADMISSION (July 31, 1942).—The patient was deeply jaundiced and thin, having lost 1 st. in the last three months. The liver was considerably enlarged, and the lower border was 4 in. below the costal margin. Its surface felt smooth and uniform, though firmer than normal. The gall-bladder was not palpable. Blood-count: R.B.C 3,720,000, Hb 64 per cent, C.I. 0·87, W.B.C. 9,600. The patient was prepared for operation by vitamin K.

FIRST OPERATION (Aug. 7).—General anæsthesia. A right paramedian incision was made above the umbilicus. A distended gall-bladder was found, obscured by the large liver. A sessile, fleshy growth was projecting into the second part of the duodenum on its medial aspect. The common and hepatic ducts were greatly dilated. The liver was free from palpable secondaries. The head of the pancreas felt normal. An anastomosis was made between the fundus of the gall-bladder and the prepyloric part of the stomach. Posterior gastrojejunostomy was then performed. The patient recovered well from this operation and the jaundice soon disappeared.

SECOND OPERATION (Aug. 25).—General anæsthesia. A rather low paramedian incision was made. Adhesions caused little trouble. The duodenum and head of the pancreas were mobilized and the duodenum was divided between clamps at the junction of the first and second parts and of the second and third parts. The head of the pancreas was next divided between artery forceps along a line 1 in. medial to the second part of the duodenum. The duct of Wirsung was not clearly identified. The dilated common duct was divided behind the first part of the duodenum and tied. The second part of the duodenum and portion of pancreas were then removed. The pancreatic tissue in the grip of the artery forceps was tied with thread, and the two ends of the divided duodenum were closed with two layers of thread suture. Some thread sutures were inserted to close the divided head of the pancreas and a drain left down to the pancreas. Intravenous glucose-saline was given for forty-eight hours.

There was only a trifling escape of pancreatic juice from the wound for two days and recovery was uneventful.

Examination of the fæces on Aug. 31, six days after the second operation, gave the following result: Total fat 58 per cent by weight of dried fæces; split fat 83 per cent of the total fat, unsplit fat 17 per cent. The patient's condition improved rapidly and he gained 1½ st. in weight in the next three months on a normal mixed diet without any pancreatic ferments or predigested food.

Eight months after the second operation he reported with obvious secondary growths in the liver, and a return of the jaundice with ascites. He died a few weeks later.

Case 2.—A man, aged 60 gave a history of a shivering attack followed by jaundice fifteen months before. There was no pain and the jaundice gradually cleared. Three months before admission he had another shivering attack followed by jaundice, which cleared after a week. One month before admission he had a similar attack, and yet another a week later. Since then the jaundice had not cleared, but had grown steadily deeper. There had been no pain throughout the illness.

Previous Health.—He had rheumatic fever at the age of 32 and had had a mitral lesion since.

ON ADMISSION.—The patient was a stout plethoric man with a pronounced golden-yellow jaundice. He had a systolic murmur at the apex. The liver was considerably enlarged. The gall-bladder was not palpable. On X-ray examination before admission the gall-bladder failed to outline. There were no shadows to suggest a stone.

Prothrombin time normal. Blood-count: R.B.C. 4,070,000, Hb 78 per cent, C.I. 0·95, W.B.C. 10,200.

DIAGNOSIS.—In view of the repeated rigors and history of intermittent jaundice, stones in the common bile-duct were considered probable, in spite of the absence of pain. Exploration was advised.

FIRST OPERATION (July 31, 1943).—General anæsthesia. Right paramedian incision. A distended gall-bladder was found behind the enlarged liver. There were no stones. A fleshy growth was felt projecting into the duodenum from Vater's ampulla. There were no enlarged lymphatic glands and no secondary growths in the liver. Cholecystogastrostomy and posterior gastro-jejunostomy were performed. Recovery from this operation was satisfactory and the jaundice soon cleared.

SECOND OPERATION (Sept. 5).—General anæsthesia. Through a transverse incision the duodenum and head of the pancreas were exposed and mobilized. The second part of the duodenum and a portion of the head of the pancreas were resected as in *Case* 1 and the ends of the duodenum invaginated.

After the operation, in spite of intravenous saline and glucose, the pulse became more rapid and weaker, and next day the patient presented a clinical picture of acute pancreatitis, with some cyanosis, persistent vomiting, and a failing circulation. He died in forty-eight hours. No post-mortem examination was made.

Recovery was uneventful, and the patient gained weight considerably in the next few months. Ten months after the second operation he reported with a slight loss of weight and what appeared to be a secondary nodule in the liver. He went down hill steadily after this and a month later committed suicide. Recurrence in the liver was found post mortem.

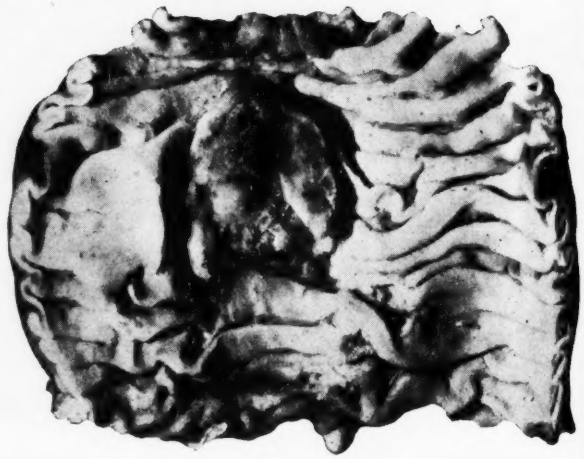

FIG. 153.—*Case* 3. The specimen.

Case 4.—A married woman, aged 68, had been losing weight for six months, with progressively deepening jaundice for the last four months, and severe pruritus. There had been no pain.

A B C

FIG. 154.—*Case* 4. A, Anterior view of duodenum and pancreas removed; B, Posterior view showing divided common bile-duct; C, Duodenum laid open, exposing growth.

Case 3.—A man, aged 46, gave a history of six weeks' epigastric discomfort and four weeks' steadily increasing jaundice with pale constipated motions. His appetite had failed and he had lost 7 lb. in the six weeks.

ON ADMISSION.—Jaundice was not very deep. The liver was enlarged and the gall-bladder doubtfully palpable.

FIRST OPERATION (Aug. 10, Mr. A. N. Guthkelch).—Right paramedian incision. The gall-bladder was distended. A firm nodular growth was felt at the ampulla of Vater, fairly mobile. Cholecystogastrostomy and gastro-jejunostomy were performed. The patient recovered well from this operation.

SECOND OPERATION (Sept. 17, J. M.).—A transverse incision was made at the subcostal plane, and the second part of the duodenum and a portion of the head of the pancreas resected (*Fig.* 153), with ligature and division of bile and pancreatic ducts.

ON ADMISSION.—The patient was very emaciated and of a deep olive-green colour. The liver was enlarged and the gall-bladder palpable. The hæmoglobin was 65 per cent.

FIRST OPERATION (Dec. 31, 1945).—Pre-operative preparation with vitamin K. Right paramedian incision. The gall-bladder was distended and also the common and hepatic ducts, which were an inch in diameter. A small soft growth could be palpated at Vater's ampulla. There were no secondaries in the liver. It was not considered wise to attempt more than a cholecystogastrostomy in order to relieve the jaundice at this stage.

The patient made a steady recovery and went home for two months to build up her reserves.

SECOND OPERATION (March 3, 1946).—Cyclopropane anæsthesia. Right paramedian incision. The duodenum and head of the pancreas were first mobilized and freedom

from secondaries was verified. A posterior gastrojejunostomy was done. Resection of the whole of the second part of the duodenum and a portion of the head of the pancreas was carried out. A drain was left to the site of resection. (*Fig.* 154.)

Owing to a tear in the duodenum during the invagination, a duodenal fistula with copious discharge of bile gave trouble for a week. It then closed and she improved rapidly. She went home with the wound soundly healed on March 26, in good general condition.

Some six weeks later she began to suffer from severe attacks of vomiting which necessitated her re-admission to hospital in a very emaciated and dehydrated condition. On intravenous plasma and saline with gastric suction she improved somewhat for three days, but then developed a bronchopneumonia which proved rapidly fatal. No post-mortem examination was allowed.

Case 5.—A widow, aged 64. History of vague indigestion and flatulence for two years, and three months' painless jaundice of increasing intensity with loss of weight and pruritus.

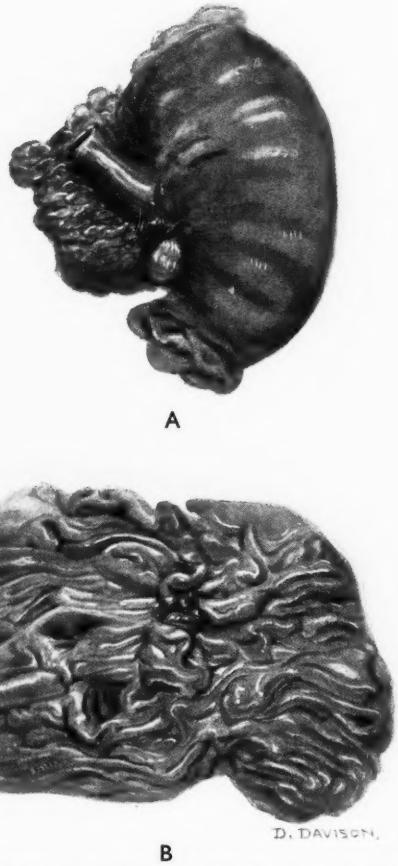

FIG. 155.—*Case* 5. A, Posterior view of specimen showing common bile-duct; B, Duodenum laid open, exposing growth.

ON ADMISSION.—The liver was moderately enlarged and the gall-bladder palpably distended. The patient was prepared with vitamin-K injections for two days.

Prothrombin time normal. Blood-urea 30 mg. per 100 c.c. Cephalin cholesterol test for liver damage negative. Alkaline phosphatase 54 units per 100 c.c.

FIRST OPERATION (March 8, 1946).—General anæsthesia. Right paramedian incision. The gall-bladder and common duct were very distended. A small growth at Vater's ampulla could be palpated. Cholecystogastrostomy and gastrojejunostomy were performed. Recovery was uneventful and the jaundice cleared rapidly.

SECOND OPERATION (April 5).—Right paramedian incision. Resection of second part of duodenum and portion of head of pancreas with division and ligature of bile and pancreatic ducts. Drain to site of resection. (*Fig.* 155.)

There was a moderate escape of bile-stained fluid for a while, but the wound was quite dry in a fortnight. The patient put on weight considerably and is now, eleven months after the second operation, in excellent health.

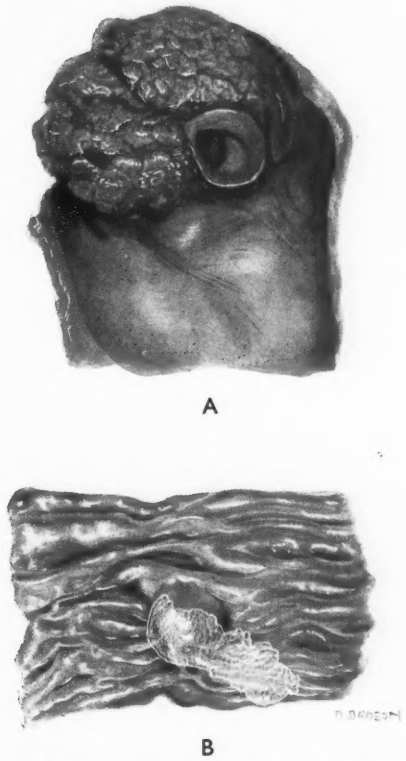

FIG. 156.—*Case* 6. A, Posterior view showing divided common bile-duct; B, Duodenum laid open, exposing growth.

Case 6.—An unmarried woman, aged 67. Admitted with six months' jaundice and loss of weight, severe pruritus, and occasional vomiting, with rigors at intervals. For eighteen months she had complained of weakness and lethargy. There had been no pain.

ON ADMISSION.—Patient was ill and drowsy and having occasional rigors. She was very wasted and had a deep olive-green jaundice. The liver was moderately enlarged and the gall-bladder palpably distended.

Radiography revealed no abnormality in the duodenal loop. Blood-count: R.B.C. 4,210,000, Hb 76 per cent, C.I. 0·8, W.B.C. 8200.

FIRST OPERATION (May 16, 1946).—Right paramedian incision. A sessile fungating growth the size of a hazelnut was felt at Vater's ampulla. The dilated gall-bladder was anastomosed with the stomach, but in view of her poor condition it was considered wise to defer the gastrojejunostomy to a later stage. Improvement was very satisfactory, and the jaundice soon cleared.

SECOND OPERATION (June 21).—Right paramedian incision. There was some trouble from adhesions, and in separating them the colon was torn slightly and repaired. Posterior gastrojejunostomy was done, and the duodenum and pancreas mobilized. The whole of the second part

of the duodenum with a portion of the head of the pancreas was removed and the bile and pancreatic ducts tied with linen thread. Drain to the site of the resection. (*Fig.* 156.) She recovered well from this operation without any appreciable leakage of bile or pancreatic juice, and soon began to put on weight. She was re-admitted to the medical wards under Dr. Holmes in January, 1947, suffering from recurrent rigors with smooth enlargement of the liver and a leucocytosis of 19,000. There has been marked improvement after treatment by penicillin, but there is little doubt that she is suffering from ascending cholangitis.

To summarize the six cases: There was one death as the direct result of operation—*Case* 2, who developed acute pancreatitis. *Case* 4 did well at first and left the nursing home in good condition, but was re-admitted six weeks later with persistent vomiting of obstructive type and died without operation being possible. Two cases developed hepatic metastasis within the year and died. One is ill from ascending cholangitis some seven months after the operation, and one is well eleven months after the second operation.

DISCUSSION

Should the Operation be done in One or Two Stages ?—Whipple, who as a pioneer in pancreatic surgery stands far above all rivals, has largely abandoned the two-stage operation he described in 1935 and now performs mainly a one-stage procedure. In his last paper (1946) he states he has done 8 two-stage and 21 one-stage operations for ampullary carcinoma or carcinoma of the head of the pancreas. In this paper Whipple gives a comprehensive account of the evolution of these operations, which makes it unnecessary to cover the same ground here. An even fuller historical summary of this subject is given in a recent paper by d'Offay (1946).

Whipple prefers the one-stage operation for the following reasons: (1) The introduction of vitamin-K therapy has removed the danger, except in severe liver damage, of post-operative hæmorrhage, once the bugbear of operation on these jaundiced patients. For this reason he lays it down that the prothrombin-time estimation and the hippuric acid excretion test should be carried out before the operation. (2) The danger of two anæsthetics is avoided. (3) The difficulty of adhesions at the second stage is obviated.

I am conscious that to report 6 cases all done in two stages may seem to stamp me as hopelessly old-fangled and out of the modern movement. But, while I do not wish in any way to decry the one-stage operation in suitable circumstances, there is something to be said for the two-stage procedure in my cases. Two patients were so ill, and appeared such bad risks, that I did not dare to do more than a cholecystogastrostomy at the first stage, and had to leave the gastrojejunostomy to be done at the second stage along with the resection. I think these two would certainly have died under a one-stage operation. But in the other four my assessment of their clinical condition led me to believe that they had more chance of survival with a two-stage than a one-stage operation. It must be remembered that the one-stage operation takes, according to Whipple, from 3½ to 5 hours to perform, and that is a severe ordeal for a patient who is emaciated, exhausted, and deeply jaundiced. My two stages took about 1¼ hours each on the average, and did not cause any severe shock. I attach little importance to the danger of two anæsthetics. Adhesions can be a nuisance at the second operation, and in one case I tore the colon slightly as a result of them, but it was easily repaired and no harm resulted.

Method of Restoration of the Flow of Bile.—Whipple now maintains that the gall-bladder should not be used to restore the flow of bile into the alimentary tract, but he advocates instead an anastomosis of the divided common bile-duct with the jejunum, on the ground that there is less risk of biliary fistula than when the upper end of the common duct is tied, and also less risk of septic cholangitis.

As to biliary fistula, the only serious one in my cases came from a tear in the duodenum and was really a duodenal fistula. It healed in about a week. I had no trouble from slipping of the thread ligature applied to the common duct. My sixth case has now developed severe cholangitis. This might possibly have been avoided had I done an anastomosis of the jejunum 'en-Y' plus a choledochojejunostomy as in Whipple's latest procedure, but I think that any artificial anastomosis between the biliary and the alimentary tract must carry some risk of ascending cholangitis. Whipple attributed his failures in cholecystogastrostomy both to particulate matter from the stomach getting into the gall-bladder and to the tendency of the stoma between gall-bladder and stomach to stenose. These seem to me to be mutually incompatible reasons, since the greater the stenosis, the less the chance there is for food particles to enter the gall-bladder. I make a rather small cholecystogastrostomy about 1½ cm. long in the belief that it will remain adequate for the escape of bile into the stomach.

Ligature or Anastomosis of the Pancreatic Duct ?—Whipple has now abandoned ligature of the pancreatic duct and has reverted to implanting it into the jejunum. He does this because of the danger of fatty degeneration of the liver, and of impaired digestion of fats, proteins, and carbohydrates resulting from ligature of the duct. I feel that there are sound reasons for caution before we accept this argument too readily. There is a risk in tying the pancreatic duct, as my second case, which developed fatal acute pancreatitis, demonstrated, but the available evidence suggests that this risk is not a heavy one, and my 5 cases that survived the resection (including the woman who died of a mysterious intestinal obstruction some two months later) all gained weight in a most satisfactory way on an ordinary diet without the use of pancreatic extract. There was not even evidence of any serious failure in fat absorption. To my mind it is a most fascinating example of the power of compensation in the human body, that the most powerful digestive juices we possess, trypsin, lipase, and amylase, can be completely witheld by ligature of the pancreatic duct, and yet the small intestine smoothly and efficiently rises to the occasion, so that the individual's nutrition does not suffer.

Although I have not yet tried it, I suspect that anastomosis of the pancreatic duct with the jejunum is technically a very difficult operation, because the obstructed pancreatic duct does not dilate as does the obstructed common bile-duct. Many of the earlier attempts at radical surgery for these growths

foundered upon the rock of pancreatic fistula, and I believe that ligature of the pancreatic duct may prove on balance to be a safer procedure than its anastomosis with the jejunum.

A CASE OF SPONTANEOUS CURE OF AMPULLARY CARCINOMA

Finally, I record a case with a somewhat different interest, which first focused my attention on this field.

In May, 1924, a woman, aged 48, was referred to me with deep jaundice of a few weeks' standing, severe pruritus, and a palpably enlarged gall-bladder. On exploring her abdomen I felt a small fleshy growth the size of a cherry at Vater's ampulla. Cholecystogastrostomy was done to relieve her jaundice, and two months later, when her condition had improved greatly, I decided to attempt a transduodenal resection of the growth. At the second laparotomy to my great surprise I could no longer feel the growth at the ampulla. I was certain it had not been an impacted gall-stone and was at a loss to account for its disappearance. I did not open the duodenum, but finding a small, normal-looking lymph-gland lying in front of the head of the pancreas to the medial side of the second part of the duodenum, I removed it for section. It proved to be stuffed with secondary spheroidal-celled carcinoma. I followed the patient up for some ten years, during which she remained in good health, and then lost trace of her. The other week I heard from Dr. Livingstone, of Hollinwood, that she had died of coronary thrombosis in 1944, twenty years after the operation, with no evidence of recurrence. It is the most convincing case of a natural cure of cancer that I have met.

SUMMARY

1. Six cases of carcinoma of the ampulla of Vater treated by a radical two-stage operation with ligature of the pancreatic duct are recorded.

2. The relative merits of the one-stage and the two-stage operation are discussed.

3. One case of apparent spontaneous cure of an ampullary carcinoma is recorded.

I am indebted to Miss. D. Davison for the water-colour and line drawings.

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THE USE OF AUTOGENOUS GRAFTS FOR THE REPAIR OF LARGE GAPS IN PERIPHERAL NERVES*

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THE repair of large gaps is the thorniest problem in the surgery of peripheral nerve injuries. During the war of 1914-18 the greatest achievement was the perfection of what is now the standard method of repair—namely, mobilization of the nerve-stumps, resection back to healthy bundles centrally and peripherally, and end-to-end suture with the limb in a position that permits easy approximation. Very large gaps have been closed in this way and it was generally thought that the subsequent stretching of the nerve, if carried out slowly and deliberately, was in no way inimical to success. Unfortunately, recent experience (Highet and Holmes, 1943; Highet and Sanders, 1943) has shown that if the gap closed is large, say 11 cm. in the case of the lateral popliteal nerve or 9 cm. in the case of the median, the post-operative stretching, however carefully carried out, damages the nerve by traction to such an extent as to preclude useful recovery. Thus the biological limit of closure is more strict than the anatomical, and to the cases in which suture is absolutely precluded must now be added those in which the operation is possible but undesirable.

Some idea of the extent of the problem is given by the following figures (*Table I*), which are based on experience gained in the treatment of some 2500 cases that have passed through the Peripheral Nerve Injury Centre at Oxford. Some kind of surgical repair was required in rather more than one-third of all cases. Ordinary end-to-end suture was performed in 71 per cent, though it must be confessed that in the early days, in our ignorance, we closed gaps that were dangerously large—with the disappointing results already reported by Highet and Holmes. Extraordinary measures are, therefore, required in at least one-quarter of all cases in which surgical repair is necessary. In our series bulb suture was performed in 0·4 per cent, suture with bone shortening in 0·4 per cent, and some kind of grafting operation was employed in 8·6 per cent. In 19.5 per cent it was found that nothing could be done because the gap was too great. It follows that whereas one case in four cannot be dealt with by ordinary end-to-end suture, there is only one case in eight in which extraordinary measures of nerve repair are technically possible. These figures are based on experience gained during a period of

Table I.—EXTENT OF PROBLEM

(Based on a study (1940–46) of 1681 of our cases, of which 41·5 per cent required surgical repair)

		Number	*Percentage*
1. Suture		499	71
2. Bulb suture		3	0·4
3. Bone shortening and nerve suture		3	0·4
4. Grafts		59	8·6
5. Extensive gap	Repair impossible	107	15·5
6. Extensive traction lesion	Repair impossible	28	4·0
		699	

* Short accounts of this work were presented at the centennial meeting of the American Medical Association, Atlantic City, June, 1947, and at a meeting of the Association of Surgeons of Great Britain and Ireland, held at Oxford in July, 1947.

experimentation; if it can be shown that the special measures employed—among which nerve-grafting is the most important—have been attended with fair success, then there is perhaps some prospect of widening the field of application. Bulb suture and bone shortening are only of occasional value; they leave the hard core of the problem untouched, and, so far as one can see, the ultimate hope lies in some form of nerve-grafting.

Heterogenous nerve-grafting has been such an unqualified failure as no longer to call for serious consideration. Fresh and stored homografts have been tried and found wanting (Seddon and Holmes, 1944; Spurling, Lyons, Whitcomb, and Woodhall, 1945; and Barnes, Bacsich, Wyburn, and Kerr, 1946). Interest in formol-fixed homografts has recently been revived by Propper-Graschenkov (1942), but the results of his work, which is biologically unsound, have also been disappointing. There are, likewise, no reports of the successful clinical application of Weiss's (1943, a, 1943, b; Weiss and Taylor, 1943) frozen-dried homografts; and recent experimental work by F. K. Sanders (to be published) has given discouraging results. We have no experience in the use of heterogenous and homogenous grafts prepared by the method of Schabadasch (1944)—removal of lipoids, and impregnation of the graft with a solution containing glucose and magnesium glycerophosphate. Grafts prepared in this way were employed in 17 clinical cases, but when his paper was written (April, 1943) the period of post-operative observation was still short. So far as I am aware no further report has been published. Thus our attention must remain focused on a method which of necessity has only a limited application—namely, autogenous grafting.

The success of nerve autografts in experimental animals is no longer in doubt. The evidence has been well presented by Sanders (1942); and in the same year Gutmann and Sanders (1942) reported the results of experiments that are of particular interest to clinicians. They estimated quantitatively the functional recovery that occurs after nerve-grafting of various kinds; in the rabbit the recovery occurring after the insertion of a 2-cm. autograft into a gap in the lateral popliteal nerve was as satisfactory as that seen after end-to-end suture.

Unfortunately the history of the clinical application of autogenous nerve-grafting inspires less confidence. A review of the results obtained up to 1939 will also be found in Sanders's (1942) paper; apart from the pioneer work of Bunnell (1927) on digital nerve-grafting, and of Ballance and Duel (1932) and Bunnell (1937) on facial nerve-grafting (Bunnell's patient was operated on in December, 1903) there was little to encourage surgeons to revise the adverse opinion that had prevailed, at any rate in Great Britain, since the war of 1914-18. Clinicians insisted, and rightly so, that they were interested only in results that were obviously beneficial to the patient. The return of feeble voluntary power to a previously paralysed muscle, though unimpeachable evidence of regeneration through a graft, was only of academic interest. The operation could not be recommended until it could be shown that a useful return of motor power or of cutaneous sensibility could be counted on in a fair proportion of cases. Nevertheless, since grafting of the facial nerve has become a generally accepted procedure there is no very clear reason why grafts should not succeed when implanted into peripheral nerves. In 1939 Bunnell and Boyes described five cases of grafting in main nerve-trunks and although the documentation of the results lacks detail it seems evident that there was worthwhile recovery in every case. In 1943 Klar reported 21 cases; as in Bunnell's series, strands of cutaneous nerve were used in every case except one, in which a segment of an irreparably damaged ulnar nerve was employed to bridge a gap in the median. The results were grouped in three classes; if all muscles were acting the case was listed as showing recovery; if at least one muscle was acting it was listed as showing improvement; the rest were failures. Of the 21 cases 5 showed recovery and 5 improvement. In 4 cases the period of post-operative observation was too short to permit a definite assessment being made, and in 3 a vascular lesion (injury to the axillary artery) had occurred and was thought to have delayed recovery. Klar considered the length of the graft of some importance. Although 1 case in which a graft 8 cm. long had been used showed recovery, he thought that the prospects were poor with grafts more than 6 cm. in length. One case in which the graft was 14 cm. long proved a failure. Unfortunately Klar was often content to use grafts of a diameter considerably less than that of the recipient nerve, which must have affected the results adversely. The cross-section area of the graft sets a strict limit to the number of fibres that can be conveyed to the peripheral stump. Another disappointing feature of Klar's report is the inadequacy of his grading of recovery. Even if all muscles were working they might still be too feeble to be of much value functionally; estimates of recovery must be quantitative.

During the same period histological evidence of regeneration through grafts in a limb was provided by Seddon, Young, and Holmes (1942), and by Barnes, Bacsich, and Wyburn (1945).

The purpose of this paper is to report the functional results after nerve autografting in 58 cases, and to show that in the absence of certain unfavourable conditions the operation can be relied on to give results not inferior to those seen after a well-executed end-to-end suture.

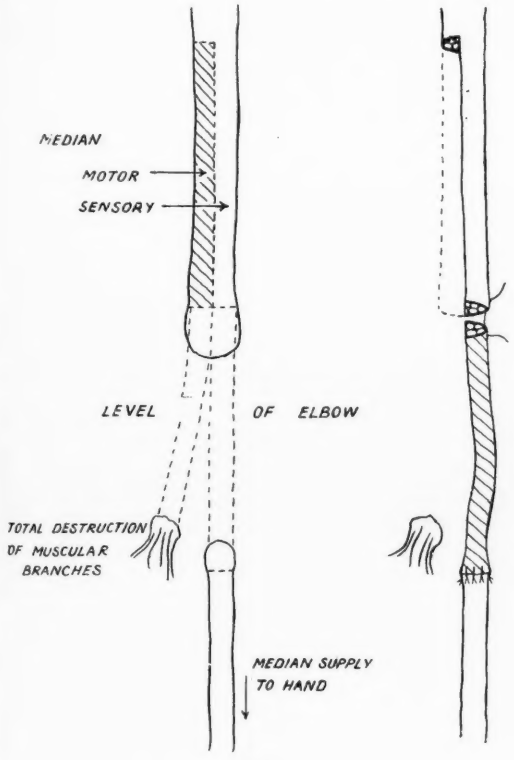
TECHNICAL CONSIDERATIONS

The Donor Nerve.—The most serious limitation in the clinical application of nerve autografting is that of obtaining sufficient peripheral nervous tissue from the patient to close a large gap in a nerve of considerable diameter. The aim must always be to implant a graft, or collection of grafts, having a total cross-section area at least equal to that of the peripheral stump of the damaged nerve. Failure to observe this obvious and elementary rule is, in part, responsible for some of the poor results that have been reported. The exiguity of supply often leaves the surgeon with no choice of materials—he must take what is available—but certain points are worth bearing in mind.

If a *cutaneous nerve* is to be used it should not be one that has entered its zone of distribution—for

example, the lateral cutaneous nerve of the thigh below the anterior superior iliac spine, or the small sciatic below the gluteal fold. Nerves such as these give off branches throughout their course, with the result that the peripheral diameter is much smaller than the proximal. There are four ideal cutaneous nerves; the internal cutaneous of the forearm proximal to its bifurcation at the elbow, the available length ranging from 20 to 27 cm.; the superficial radial nerve between the elbow and the wrist, yielding a length of 20 to 25 cm.; the sural (external saphenous) between its origin and the lateral malleolus, yielding a length of 25 to 40 cm.; and the (internal) saphenous in the thigh—up to 40 cm. (d'Aubigné, 1946). Before using the sural nerve it was formerly our custom to carry out a block with a local anæsthetic in order to determine whether the resulting zone of insensibility extended on to the heel. In no case was there any such extension and therefore there is probably no risk of trophic ulceration following resection of the sural nerve. The superficial radial nerve should not be used for repair of the median unless the donor nerve is irreparably damaged. If the superficial radial nerve is excised on the injured side then the patient is deprived of such benefits as would result from sensory overlapping from the superficial radial into the median area. If the contralateral superficial radial nerve is used the patient will then have two subnormal hands instead of one.

All four nerves recommended have much the same diameter, about 3 × 2 mm.



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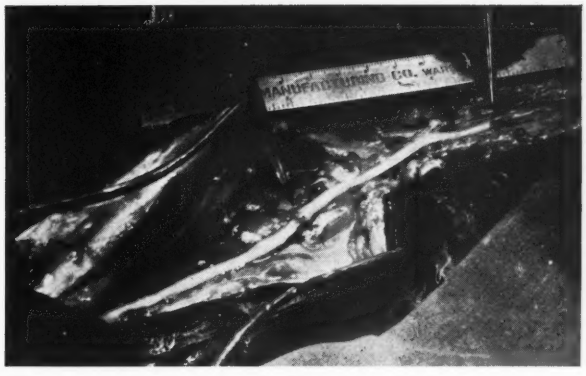


B

FIG. 157.—A, Diagram of operation in which one-half of the trunk of the median nerve was used for repair of the other. B, The graft in situ (E.12, *Table V*).

There is a theoretical objection (Gutmann and Sanders, 1943) to the use of cutaneous nerves for the repair of nerves containing motor-fibres. Since much the largest nerve-fibres are the motor and proprioceptive, the fibres present in cutaneous nerves are never of a size equal to that of the largest fibres in a mixed or motor nerve. It might, therefore, be thought that motor recovery through a cutaneous nerve-graft would be appreciably inferior to the sensory recovery. The evidence presented by our series of cases shows that this possible objection has little substance; and Simpson and Young (1945) have shown that large fibres in the central stump have no difficulty in inflating rather small peripheral tubes, and so attaining a diameter sufficient for their effective function.

Table II.—SOURCES OF MATERIAL USED FOR GRAFTING

Cutaneous Nerves:—	
Medial cutaneous of forearm	21
Sural	9
Superficial radial	7
Others	3
Main Trunk:—	
Ulnar	8
Lateral poplitea	4
Half thickness median	3
Radial	2
Others	4
	61

Other small nerves (*see Table II*) have been used in exceptional cases, the reasons for employing them being their ready availability or the fact that they also had been severed and could not be repaired.

A *segment of a trunk of a main nerve* may be used in a case where two main nerves have been so extensively damaged that neither can be repaired by end-to-end suture, or where the function of one nerve is so predominantly important that it is justifiable to take a graft from the other for its repair even though suture of the less important is possible. Since our results have led us to believe that main-trunk grafting of the median nerve is a fairly reliable procedure, it might even be justifiable to take a segment from an intact radial nerve for repair of a large gap in the median, though we have not yet ventured on such a drastic procedure. As will be seen from *Table II* the ulnar has been used most frequently as a graft; the radial, the lateral popliteal, and even the whole sciatic have also been employed, and in three

cases (*Fig.* 157) the median nerve itself has been split in order to provide a graft for repair of the other half of the nerve, in which there was some prospect of restoring function.

An objection to the use of main-trunk grafts is the risk of more or less necrosis; it has certainly been reported (Sanders, 1942), and was observed in one of our cases (*Table VI, Case* A.35; Holmes, 1947). Yet histological observations made by Barnes et al. (1945) and Holmes (1947) show that a large graft may survive. There may well be a critical diameter which it is unwise to exceed, and it is possible that the size of the lateral popliteal nerve, the largest we have employed apart from the one main sciatic graft, exceeds the limit of safety. There was undoubted evidence of ischæmic change in one lateral popliteal graft and the clinical results in all but one case have been disappointing. Perhaps the ingenious nerve pedicle grafting operation described by Strange (1947) should be employed where grafts of large diameter are used. However, the clinical evidence of recovery after main-trunk grafts in the upper limb is such that the degree of ischæmic change in the graft is of no great significance.

The possible merits of *predegenerate grafts* have frequently been debated and there are two reasons why they might be superior. The degenerate axons and myelin having been absorbed, there are then free channels waiting to receive the outgrowing axons; there is also a great increase in the number and activity of the Schwann cells—greatest, according to Abercrombie and Johnson (1942), between the nineteenth and twenty-fifth days—which should ensure better unions with the host nerve.

Yet Bunnell and Boyes (1939) and Sanders and Young (1942) found no significant difference in regeneration through fresh grafts compared with that seen after implantation of predegenerate ones, and on practical grounds there is much to be said against use of the latter. It is true that in a case where one has advance information of the extent of the gap to be repaired, and in consequence can predetermine the appropriate donor nerves, the small preliminary operation of severence of the donor nerve could be carried out a few weeks before the final procedure. But unfortunately the exact state of affairs is rarely known until the definitive operation, and having exposed the stumps of the damaged nerve and determined the extent of the damage one would then hardly be justified in closing the wound, dividing the donor nerve, and performing a second major operation three or four weeks later. The lateral popliteal graft may be a special case. The one example of necrosis that we have seen occurred in a graft taken from the central stump of the lateral popliteal nerve (Holmes, 1947), whereas the graft taken from the peripheral stump of the same nerve, seven months after injury, showed no necrosis and contained regenerating fibres of large size.

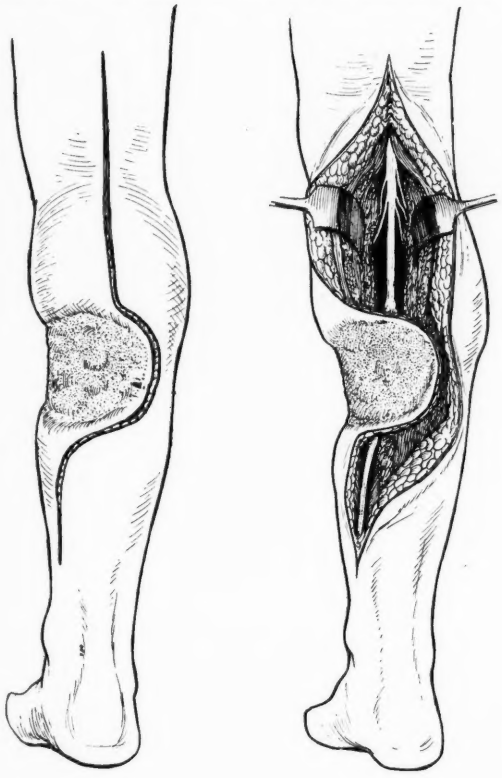
In a number of cases we were compelled by circumstances to use the peripheral and therefore degenerate stump of a divided nerve as a graft. In these cases degeneration dated from the original injury and was often of many months' standing. The final results in these cases were not altogether encouraging, and it is possible that longstanding degeneration of a graft is positively harmful, on account of the considerable shrinkage of the Schwann tubes (Holmes and Young, 1942; Sanders and Young, 1944) having prevented the outgrowing nerve-fibres from attaining diameters adequate for satisfactory function. In the case described by Barnes et al. (1945) the graft taken from the peripheral stump of the ulnar nerve 613 days after injury was found to contain only very small fibres, all unmedullated. The poor condition of the fibres was ascribed to the extensive intrafascicular collagenization. In one of our digital nerve cases, two of the grafts were fresh and two had been degenerate for nine months; satisfactory regeneration occurred through the former but not through the latter. There was no excessive collagenization of the stumps of the recipient nerves and it is, therefore, possible that failure was due to the state of the grafts. Yet in this and other similar cases the shrinkage of Schwann tubes in the donor nerve cannot have exceeded that in the peripheral stump of the recipient: this explanation is inadequate unless the temporary devascularization of the graft consequent on its resection greatly aggravates the shrinkage.

Operative Procedure.—The technique of autogenous nerve-grafting is essentially similar to that required for ordinary secondary suture, and discussion will be limited to those points that are of particular importance.

1. *Cutaneous Scarring.*—Since the wounds of nerves that call for repair by grafting are usually extensive the need for the replacement of skin scars by healthy tissue arises with corresponding frequency. Nothing less than a full-thickness flap or tube pedicle graft will suffice since it is important that the graft should lie, so far as possible, in healthy well-vascularized tissue. There are, however, circumstances in which it is justifiable to leave the scar untouched, as will be explained below. When the first operation for plastic repair of the skin is undertaken the stumps of the divided nerve should be exposed. This will enable the surgeon to determine the extent of the gap and so estimate whether the nerve can be repaired by secondary suture or by grafting. If the gap is too great to be closed by any means, then there will probably be no point in proceeding with an elaborate plastic skin repair; replacement of the scar by a split skin-graft will suffice. The plastic repair, if indicated, should be carried to a conclusion as rapidly as possible so as not to add unduly to the delay between the original injury and the final repair of the nerve.

2. *Exposure of the Nerve: Mobilization of the Stumps.*—The technique is the same as that required for ordinary secondary suture, except that there will be no need to prolong the incision for mobilization of the stumps unless the gap is so great that, with the supply of graft material at the surgeon's disposal, it cannot be closed by grafting alone. He must then consider whether reduction of the gap by full mobilization of the stumps will bring grafting within the range of possibility. If there is a reasonable prospect of success, full mobilization of the stumps is carried out and, after they have been approximated as much as possible, the neighbouring joint being flexed to a convenient degree, the remaining gap is bridged by grafting.

3. *Suture possible but undesirable.*—Here it is convenient to consider the case in which suture is anatomically possible but undesirable on account of the degree of flexion necessary to bring the resected stumps together. It has already been shown that serious damage may be inflicted on a nerve sutured in extreme flexion by the stretching required to straighten the limb subsequently (p. 151). As a practical guide it may be said that more than 90° flexion of the knee or the elbow is dangerous. The proper procedure is to flex the joint to 70° to 90° to approximate the stumps as much as possible, and bridge whatever gap remains by means of a graft.



4. *Resection of the End-bulbs.*—There is rarely any risk of inadequate resection of the central stump since the very existence of a neuroma is an indication that it contains healthy axons. Resection at the upper limit of the neuroma generally ensures the exposure of bundles that have not been affected by retrograde degeneration, and the junction of neuroma with the nerve-trunk above is, therefore, the site of election. Where the neuroma is buried in scar there is still no difficulty. For on cutting the nerve across one can easily recognize the translucent mobile bundles of a healthy central stump. Unfortunately, the peripheral stump cannot be approached with the same certainty, since, as will be described more fully later (pp. 157, 158), there may be serious collagenization within the bundles of the peripheral stump (Holmes, 1947), which often cannot be recognized by the naked eye. The distal resection should, therefore, err on the side of generosity, especially in the digital nerves. This recommendation is of course based on the assumption that the collagenization is of limited extent (*see* Holmes, 1947).

5. *The Bed for the Graft.*—Although there is no doubt that a graft is vascularized chiefly from the central and peripheral stumps the hazards should not be gratuitously increased by allowing it to lie in a badly scarred bed. Every attempt must be made to excise scar tissue and if the difficulties are insuperable the graft may sometimes be threaded beneath the scar through a tunnel of healthy tissue. This leads naturally to consideration of what may be called—

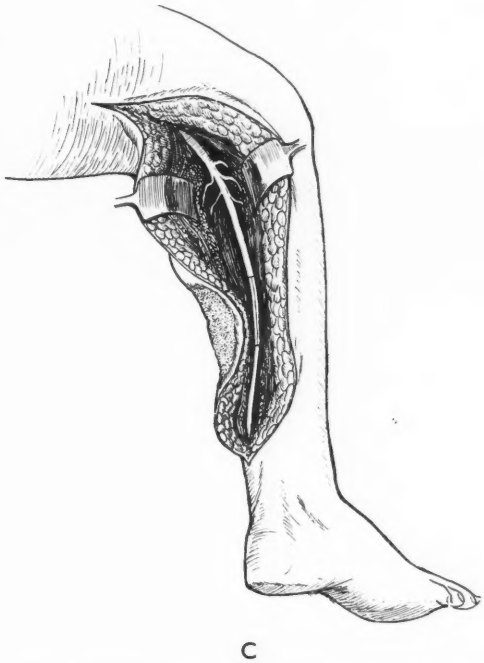


FIG. 158.—The by-pass operation. A, Skin incision carried to one side of the deep scar, through healthy tissue; B, Central and peripheral stumps isolated above and below the scar; C, After mobilization of the central stump and flexion of the knee the nerve-ends were laid in the by-pass and united with three strands of cutaneous nerve. Plasma-clot fixation. (B.146A, *Table IV.*)

6. *The By-pass Operation.*—This simple procedure may sometimes be employed with great advantage; it is best understood by reference to a particular case.

In a case of posterior tibial nerve injury (*Fig.* 158) it was known that all the structures in the calf had been divided by an enormous pressure sore. The deep scar was, therefore, left undisturbed and the stumps of the nerve were isolated above and below it. No attempt was made to perform a clean dissection of the end-bulbs and they were severed at the points where they entered the dense scar. The incisions above and below the scar were then joined by one passing well to the side of it, through healthy subcutaneous tissue and deep fascia. After resection of the stumps it was found that the gap was greater than could be closed by grafting alone, and the central stump was, therefore, mobilized to the upper end of the popliteal fossa. With the knee flexed 90° the central stump was then drawn down into the by-pass and anchored there. The gap remaining

was only 5 cm. and was easily closed with a cable of three strands taken from the fibular root of the sural nerve. (*See also Fig.* 166)

7. *Preparation of the Graft.*—After the extent of the gap to be closed has been accurately determined, a graft of appropriate length is prepared. It is now well recognized (Sanders and Young, 1942) that grafts shrink, and hence it is wise to prepare a graft about 15 per cent longer than the gap to be closed. Whether a cutaneous nerve-graft, single or in the form of a cable, or a main trunk is employed depends upon the particular circumstances. If other material is obtainable a graft should not be taken from the peripheral stump of a divided nerve if the injury had occurred more than 6 months previously; it is worth while taking extra trouble to obtain a graft either from a normal (cutaneous) nerve or from the central stump of a large nerve, if available. If, for example, the median and ulnar nerves are severely damaged in the upper part of the arm, and it is decided to use the ulnar for repair of the median the incision should be extended proximally, with division of pectoralis major, in order to obtain a graft from the central stump of the ulnar, even though it would be technically more simple to take it from the peripheral stump.

If it is decided to employ a main-trunk graft, the surgeon may well consider whether he can profitably employ Strange's (1947) pedicle technique in order to ensure an adequate blood-supply.

8. *Suture of the Graft or Grafts.*—A number of ingenious methods for suture of cable grafts have been described; they are all intricate and it must be conceded that a cutaneous nerve, on account of its loose structure and the thinness and mobility of its sheath, is hardly suitable material for precise suture with thread. Accurate fixation of small grafts has been greatly facilitated by the introduction of plasma suture (Young and Medawar, 1940) and it was in this field that the clinical application of what was at first an animal experimental technique was most welcome (Seddon and Medawar, 1942). The field of operation must be dry; fibrin foam may be employed with advantage for controlling oozing, especially that from the cut surfaces of the central and peripheral stumps. The grafts are laid in position and their ends accurately apposed with the cut surfaces of the stumps. Provided that the grafts have not been moistened with saline it will be found that they are sufficiently tacky to adhere slightly to the cut surfaces of the stumps. The operating table is then manipulated in such a way as to make the bed of the graft a horizontal lake. Bone wax or fibrin foam may be used (they are removed later) to build up any deficiency in the side of the lake so that it will form a convenient receptacle for the plasma. It has not been found convenient to use the plasma suture moulds devised by Tarlov (1944). An assistant then drops the prepared plasma from a fine pipette onto one junction, the surgeon concentrating all his attention on the line of suture. He may find it necessary to hold one or more grafts in position with watchmaker's forceps—which can be withdrawn without disturbance after the plasma has clotted. A second batch of plasma is then prepared and used for the distal suture line. In order that the grafts may acquire an adequate blood-supply from the surrounding tissue it is probably wise (Tarlov and Epstein, 1945) to avoid application of plasma to the grafts throughout their length, though in practice this is often difficult.

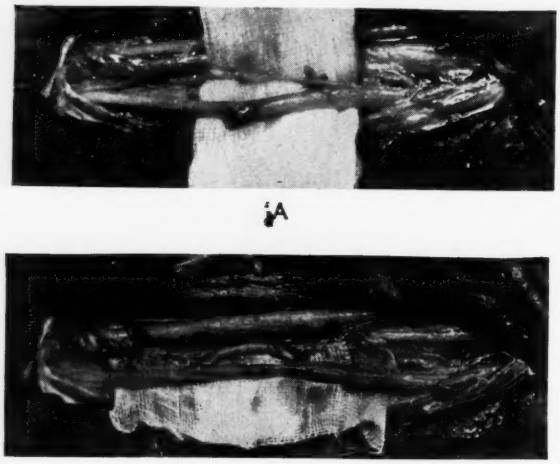


FIG. 159.—Repair of a partial division of the ulnar nerve by inlay grafting. A, The lesion. B, Separation of damaged bundles, above, from normal bundles, below; oozing from the nerve, which would obscure this delicate dissection, is controlled by Crile clamps applied to the nerve above and below the lesion. C, Nerve repaired with one strand of the medial cutaneous nerve of the forearm, which was attached to the ulnar nerve with fine stitches. The length of the graft was left attached to its bed, so that part of its blood-supply was preserved. Result: almost perfect restoration of function (J.49, *Table VII*).

A main-trunk graft may be stitched to the stumps in the ordinary way; plasma has no particular advantages, and it there is any tendency for the sheaths of the stumps or of the graft to evert it is distinctly inferior to stitches. Davis and Cleveland (1934) have recommended resection and resuture of the distal junction at about the time when the axons may be expected to have grown across the graft. They believe that invasion of the distal junction by fibrous tissue obstructs the passage of axons from the graft into the peripheral stump; the proper remedy would, therefore, be a secondary resection and suture at that level. However, since union at a suture line is brought about primarily by the outgrowth of Schwann cells, and since they grow more actively from the peripheral stump, the distal junction ought, if anything, to be more satisfactory than the proximal. Neither on experimental nor on clinical grounds have we found support for Davis and Cleveland's recommendation, and we are not impressed with the evidence they have adduced in support of it—*see* Sanders

and Young (1942). It may be that separation of the distal suture line has sometimes occurred as a result of shrinkage of the graft; as has already been indicated, this may be avoided by using grafts that are longer than the gap to be closed. All forms of nerve wrapping, such as tantalum foil, are to be avoided; they can only interfere with revascularization of the graft.

9. *The Use of Grafts for the Repair of partially divided Nerves.*—Partial suture of an incompletely divided nerve, the unaffected portion forming a lateral loop at the level of suture, is not a satisfactory procedure. There is no epineurium on the intraneural face of the resected stumps, which means that stitches inserted on this aspect will almost inevitably damage nerve-bundles; and some of the bundles, being unenclosed by epineurium, will pout laterally. The success of autogenous grafting justifies the employment of another method which is technically much more satisfactory. An example of the repair of a partially divided nerve by inlaying an autogenous graft is illustrated in *Fig.* 159.

RESULTS

The methods employed in assessing results are those recommended by the Medical Research Council and in use at the five peripheral nerve injury centres in Great Britain. Motor power is graded as :—

5 normal.
4 contraction against gravity and resistance, but less than normal.
3 contraction against gravity but not against resistance.
2 contraction, but not against gravity.
1 flicker of movement.
0 complete paralysis.

and the abbreviations used in describing muscles are :—

Radial :	B.Rad.	Brachioradialis.
	E.C.R.L.	Extensor carpi radialis longus.
	E.C.R.B.	Extensor carpi radialis brevis.
	E.D.C.	Extensor digitorum communis.
	E.Min.D.	Extensor minimi digiti.
	E.C.U.	Extensor carpi ulnaris.
	A.P.L.	Abductor pollicis longus.
	E.P.L.	Extensor pollicis longus.
	E.P.B.	Extensor pollicis brevis.
	E.I.	Extensor indicis.
Median :	P.T.	Pronator teres.
	F.C.R.	Flexor carpi radialis.
	P.L.	Palmaris longus.
	F.D.S.	Flexor digitorum sublimis.
	F.P.L.	Flexor pollicis longus.
	F.D.P.	Flexor digitorum profundus.
	P.Q.	Pronator quadratus.
	A.P.B.	Abductor pollicis brevis.
	O.P.	Opponens pollicis.
	F.P.B.	Flexor pollicis brevis.
Ulnar :	F.C.U.	Flexor carpi ulnaris.

Touch sensibility was assessed with a 1-g. von Frey hair and two-point discrimination with blunt-pointed engineer's dividers. By 'over-reaction' is meant an exaggerated, abnormal, and peculiarly unpleasant sensation provoked by a painful stimulus (what Head called protopathic pain), which often persists when recovery is incomplete.

Considerations of space have compelled one to limit the evidence of recovery to essentials. For example, in describing the return of function in the hand after grafting of the median nerve, no mention is made of sweating since recovery of this function is of little significance to the patient. There is, however, full documented evidence in every case which is at the disposal of anyone interested in the minutiæ of functional recovery.

With but few exceptions the cases presented lesions of exceptional severity. As will be seen from the tables the delay between injury and nerve repair was often prolonged, either on account of persistent infection or the need for more or less elaborate plastic skin operations which were an essential preliminary to nerve repair. In the upper limb there was injury of a main blood-vessel in no less than 12 out of 34 cases. In using such terms as 'success' and 'partial recovery' it would be justifiable to compare the results obtained with those seen after end-to-end suture of comparable nerves under equally unfavourable conditions. However, a more rigid standard of comparison has been chosen, namely, for each individual case the best result observed at the Oxford centre after secondary suture of the same nerve for repair of a short gap occurring at the same level as in the grafted case. This is an important point. It must be borne in mind that in certain situations the results of the most carefully executed end-to-end sutures, carried out under favourable conditions, always leave much to be desired; for example we have yet to see a satisfactory result after suture for a high lesion of the ulnar nerve. Clearly then it would be wholly illogical to expect anything better from a nerve-graft.

Group A : Digital Nerve-grafts (*See Table III*).—In 2 of the early cases, Mc.1 and A.12, the operations were frankly experimental, the patients' disability being very small; the men concerned were, however, anxious that something should be attempted since the loss of sensibility was just sufficient to make them conscious of a certain weakness of the hand. In no case was there prolonged sepsis nor was scarring at all excessive. In 4 cases the loss of skin was such as to require plastic repair and preliminary flap or pedicle grafts were performed. The average delay before nerve repair was considerable—10 months—and excellent recovery occurred in a case where there was a delay of 13 months (F.11). The site and extent of the nerve gaps repaired are shown in *Table III* and *Fig.* 160. The histological condition of the nerve stumps, especially the peripheral, proved to be a factor of prime importance, and a full discussion of the findings will be found in the following paper by W. Holmes. In 5 cases there was extreme endoneurial collagenization and in none has satisfactory recovery occurred. As will be explained more fully by Holmes, we associate this endoneurial scarring with the damage to the digital vessels which is almost always present. It is reasonable to suppose that in those cases in which the peripheral stumps were satisfactory, in spite of severance of the digital vessels, a satisfactory collateral circulation developed before irreversible ischæmic changes had occurred in the peripheral stumps. Thus the chief reason for failure is collagenization of the peripheral stump. There were also 2 cases, S.27 and K.30, in which no

recovery occurred although the state of the peripheral stumps was satisfactory. In these two cases something must have gone wrong at one or other of the suture lines or, for some other reason entirely unknown to us, the grafts failed to act as satisfactory

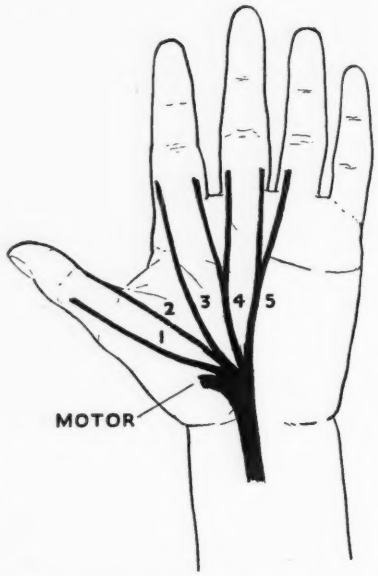


FIG. 160.—Diagram showing sites of nerve-grafting in the hand—*see Table III.*

channels for the outgrowing axons. These results are hardly as good as Bunnell's. It may be that our technique is inferior to his—on the other hand, the wounds in our small series were mostly of exceptional severity.

Group B : Cable Grafts (*See Table IV*).—The 3 brachial plexus lesions were all due to traction and the extent of the damage such that in no case was an entirely adequate resection performed. A.17 was a failure on account of undue delay between injury and repair, the paralysed muscles being extremely wasted.

The causes of the median nerve lesions were gunshot wounds 3, laceration 1, compound fracture 1 (*Fig.* 161), and a deep burn 1. In this last case (R.75)

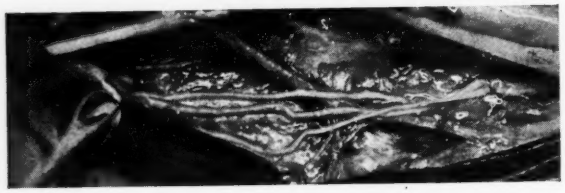


FIG. 161.—Cable graft of median nerve. Only the upper junction is shown. The plasma-clot is invisible, but its presence is indicated by the bright reflections from its surface (W.82, *Table IV*).

an extensive plastic repair was necessary and, as will be described subsequently, there was such profound collagenization of the peripheral stump as to give little expectation of recovery.

Grafting of the radial nerve is rarely required since the reconstructive treatment for the irreparable nerve lesion, tendon transplantation, is so generally satisfactory. In the three cases in which grafting operations were performed the circumstances were exceptional (*see Table IV*). In each case the cause of the nerve injury was a gunshot wound.

The one posterior tibial nerve lesion (*see* p. 155) was due to an enormous pressure sore which involved every structure in the calf. Unfortunately, as in the median nerve injury case R.75 referred to above, subsequent histological examination of the peripheral stump showed extreme endoneurial collagenization and there is, therefore, little prospect of good recovery.

Group C : Main-trunk Nerve-grafts (*See Tables V* and *VI*).—In 11 of the 13 median nerve lesions the injury was due to a gunshot wound, in 1 to traction, and in 1 to laceration of almost all the structures in the anterior compartment of the forearm. The last 2 cases will be described briefly since they illustrate how much may be retrieved in in a limb in which, at first sight, there is little hope of restoring useful function.

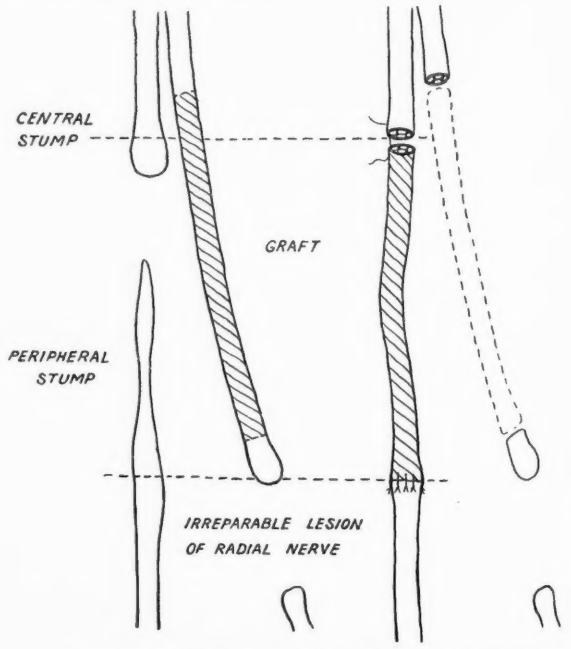


FIG. 162.—Extensive traction injury of median nerve and large gap in the radial due to an open wound. Graft from central stump of the radial used for repairing the gap in the median nerve (H.112, *Table V*).

H.112, R.A.F. officer, was shot down on July 22, 1944, when flying over enemy territory. He sustained multiple injuries which included an open supracondylar fracture of the left humerus with paralysis of all muscles below the shoulder apart from the flexors of the fourth and fifth digits. After many adventures he arrived at the Wingfield-Morris Hospital on Sept. 11.

Condition of the Left Arm on Admission.—Satisfactory union of the fracture of the lower end of the humerus; wound healed. Feeble voluntary power in the deltoid and spinati. Complete paralysis of the musculocutaneous, the radial distal to triceps, and the median nerves; feeble voluntary power in all muscles supplied by the ulnar nerve, no ulnar anæsthesia or analgesia.

Provisional Conclusion: almost certainly two separate nerve injuries, the radial being damaged at the site of fracture, the other three in the infraclavicular region. Since there was some joint stiffness and œdema, exploration was postponed until the condition of the limb was more satisfactory.

Table III.—GROUP A: DIGITAL NERVE-GRAFTS

NUMBER	DATE OF INJURY	NATURE OF INJURY	INTERVAL BEFORE HEALING (MONTHS)	DATE OF GRAFTING OPERATION	INTERVAL BETWEEN INJURY AND REPAIR (MONTHS)	EXTENT OF GAPS (CM.)						SCARRING	STATE OF PERIPHERAL STUMPS		RESULT
						Motor	Cutaneous						Collagen		
							1	2	3	4	5		Perifascicular	Intrafascicular	
Mc.1	Oct., 1938	G.S.W.	4	Sept., 1941	35	—	—	—	—	6	—	++	+++	+++	*Failure*
C.19	Aug., 1940	Bomb wound	10	July, 1941	11	—	3·5	5·7	5·1	5·5	—	++	++++	++++	*Failure*
A.12	Oct., 1940	Laceration	¾	June, 1941	8	—	—	—	—	4·5	—	++	+++	+++	*Failure*
S.27	Jan., 1941	Laceration	1	Oct., 1941	9	2·5	4	5·5	—	—	—	++	N	N	*Failure*, apart from feeble action (2) in F.P.B.
F.11	Feb., 1941	Laceration	½	March, 1942	13	—	2·8	1·5	—	—	—	++	++	N	*Success*: Recovery began after 3 mth., and by 30 mth. touch was so good that two-point discrimination was 6 mm. Overlap excluded by nerve-block
N.13	April, 1942	Laceration	1½	Jan., 1943	9	—	3·5	4	—	5·5	4·8	++	1, 2: +	1, 2: +	*Success* in 1 and 2. Recovery of pain after 9 mth. and touch after 17 mth., no over-reaction, two-point discrimination poor. *Failure* in 4 and 5
													4, 5: +++	4, 5: +++	
S.93	Aug., 1943	Bomb wound	7	June, 1944	10	—	6	7	10	8	—	++	N	N	*Success*: At 12 mth. touch and pain sense throughout, but localization poor; cross-reference of stimuli, no over-reaction
Mc.20A	Oct., 1943	Laceration	¾	May, 1944	8	—	3·5	3·5	4	—	—	++	1, 2: +++	1, 2: +++	*Partial recovery*: At 22 mth. still loss of sensibility over terminal phalanx of thumb and second and third phalanges of index on radial side
													3: N	3: ++	
L.49	Dec., 1943	Laceration	1½	Nov., 1944	11	—	—	—	4·7	0·7	—	++	+	+	*Success*: At 21 mth. touch and pain sense throughout, no over-reaction, but tactile discrimination poor
M.96	April, 1944	Laceration	½	Nov., 1944	7	—	3·5	3·7	3·5	5	—	++	+++	+++	*Failure*: Only a little return of sensibility in palm and at bases of digits
G.63	May, 1944	G.S.W.	1	Aug., 1944	3	—	3	3	2·8	2·5	2·7	++	N	N	*Partial recovery*: At 12 mth. F.P.B. 2; at 18 mth. coarse touch to tips of digits, but pain and fine touch absent at tips
R.63	June, 1944	Incised wound	½	Dec., 1944	6	—	5	5	5	—	—	o	N	N	*Success*: At 12 mth. touch and pain sense throughout; two-point discrimination 5 mm. on index, 12 mm. on thumb, no over-reaction
K.30	July, 1944	Penetrating wound	¾	May, 1945	10	—	4·5	5	7	4·8	—	+	+	+	*Probable failure*: No recovery at 17 mth.
C.134	Oct., 1944	G.S.W.	2	Jan., 1945	3	—	—	1·2	2·2	—	—	+	N	N	*Success*: At 22 mth. touch and pain sense throughout, localization good, no over-reaction, two-point discrimination poor
H.150	April, 1945	Laceration	½	June, 1946	14	—	—	—	2·8	2·4	1·6	o	N	N	*Recovering*, but too early for assessment
S.175	June, 1945	Laceration	1½	Nov., 1945	5	—	—	—	—	3	4·2	++	N	N	*Recovering*, but not well

Table IV.—GROUP B: CABLE GRAFTS

NUMBER	DATE OF INJURY	NERVE	LEVEL	INTERVAL BEFORE HEALING (MONTHS)	DATE OF GRAFTING OPERATION	INTERVAL BETWEEN INJURY AND REPAIR (MONTHS)	EXTENT OF GAP (CM.)	LEVEL OF UPPER SUTURE LINE	SCARRING	DONOR NERVE (C.S., Central Stump P.S., Peripheral Stump)	REASON FOR GRAFTING OPERATION	RESULT
C.5	Nov., 1940	Cervical 5, 6 (7)	Posterior triangle of neck	0	Jan., 1941	2	4	Transverse processes	+	Three strands of superficial radial. P.S.	End-to-end suture very difficult	*Partial recovery*: 18 mth., return of sensibility and commencing motor recovery: at 60 mth., deltoid and biceps 2½
B.27	July, 1941	Cervical 5, 6	Posterior triangle of neck	0	Feb., 1942	6½	5·5	Transverse processes	0	Three strands of normal superficial radial	End-to-end suture very difficult	*Failure*: At 36 mth., a little sensory recovery and biceps 2
A.17	Aug., 1941	Cervical 5 (6)	Posterior triangle of neck	0	May, 1943	21	5·8	Transverse process	+	Three strands of normal superficial radial	End-to-end suture very difficult	*Failure*: Severe traction lesion, late repair, extreme muscle atrophy
W.82	Nov., 1942	Median	Forearm	9	Dec., 1943	13	12	10 cm. below elbow	+	Three strands of normal sural	Precarious blood-supply making mobilization undesirable	*Success*: At 22 mth., thenars 2; return of sensibility throughout, with fair localization but slight over-reaction
Z.2	Jan., 1943	Median	Forearm	2	May, 1943	4	7·5	10·5 cm. below elbow	++	Two strands of superficial radial from normal side and P.S. anterior interosseous injured side	Large gap	*Success*: At 24 mth., good recovery, with no over-reaction and fair localization
H.133	Feb., 1944	Median	Forearm	9	Aug., 1945	18	3·4	16·5 cm. below elbow	++	Three strands C.S. superficial radial (irreparably damaged at wrist)	Large gap	*Success*: At 15 mth., light touch felt everywhere; some over-reaction to pin-prick
R.75	Aug., 1944	Median	Forearm	9	Sept., 1945	13	3·3	25·5 cm. below elbow	+	Four strands of C.S. medial cutaneous	Large gap	Will almost certainly be a *failure* on account of ischæmia of peripheral stump
S.164	Jan., 1945	Median	Forearm	4	Sept., 1945	8	6	20 cm. below elbow	+	Two strands of C.S. medial cutaneous	Large gap	*Recovering*: Well at 9 mth.; pain and coarse touch present throughout
R.78	Nov., 1945	Median	Axilla	2	Jan., 1946	2	4	32 cm. above elbow	0	Two strands of normal medial cutaneous	Large gap	*Recovering*: At 131 mth., good power in some forearm muscles, but too early for accurate assessment
S.107	Feb., 1944	Radial	Lower arm	5	Aug., 1944	6	10	4 cm. above elbow	++	Two strands of P.S. superficial radial	Joint stiffness precluded immediate tendon transplantation	*Partial recovery*: At 15 mth., E.D.C., E.C.U., and A.P.L. 2
W.123	April, 1944	Radial	Upper arm	4	March, 1945	11	6	14·5 cm. above elbow	0	One strand of C.S. medial cutaneous	Uncertainty about power of muscles for transplantation	*Recovering*: At 16 mth., E.C.R.B. 3, E.D.C., and E.Min.Dig. 2
S.131	Aug., 1944	Radial	Mid-arm	5	Feb., 1945	7	4·5	10·5 cm. above elbow	0	Three strands of C.S. medial cutaneous	Patient opposed to tendon transplantation unless nerve completely irreparable	*Success*: At 24 mth., radial extensors and extensors of digits 4; good synergic and fair independent movement
B.146A	Oct., 1944	Posterior tibial	Mid-calf	4	Aug., 1945	10	5	7 cm. above malleolus	0	Three strands of normal fibular communicating	Large gap	Will almost certainly be a *failure*, on account of ischæmia of peripheral stump. However, pin-prick appreciated in proximal two-thirds of sole at 16 mth.

Table V.—GROUP C: MAIN-TRUNK GRAFTS (MEDIAN NERVE)

NUMBER	DATE OF INJURY	LEVEL	INTERVAL BEFORE HEALING (MONTHS)	DATE OF GRAFTING OPERATION	INTERVAL BETWEEN INJURY AND REPAIR (MONTHS)	EXTENT OF GAP (CM.)	LEVEL OF UPPER SUTURE LINE: CM. ABOVE OR BELOW ELBOW	SCARRING	DONOR NERVE (C.S., Central Stump; P.S., Peripheral Stump)	REASON FOR GRAFTING OPERATION	RESULT
E.12	June, 1942	Elbow	8	July, 1943	13	7	5 above	+	Half of C.S. median	Destruction of long flexors supplied by median nerve: large gap: limited movement at elbow	*Success*: At 39 mth., A.P.B.4 (other thenar muscles supplied by ulnar nerve) recovery of sensibility, no over-reaction, localization fair, two-point discrimination average 7 mm.
W.72	Oct., 1942	Elbow	1	Sept., 1943	11	6·5	2·5 above	None	Half of C.S. median	Failure of bulb suture: partial destruction of flexors supplied by median nerve	*Success*: At 20 mth. F.P.L 4·5, P.L. 4, F.D.P. 3; recovery of sensibility in all but distal halves of digits
H.79	Nov., 1942	Lower forearm	6	Nov., 1943	12	8	25 below	+++	Half of C.S. median	Mobilization inadvisable on account of scarring	*Success*: At 24 mth. no recovery in thenar muscles, recovery of sensibility in thumb and index, two-point discrimination 3·8 cm.
S.63	Nov., 1942	Forearm	6	July, 1943	8	12	4 below	+	C.S. ulnar	Large gap in both nerves	*Success*: At 24 mth. thenar muscles 4; at 28 mth. recovery of sensibility, no over-reaction, localization poor, two-point discrimination bad
M.66	Feb., 1943	Lower forearm	8	Dec., 1943	9	7	21 below	++	C.S. ulnar	Ulnar nerve hopelessly damaged; mobilization of median undesirable on account of scarring	*Success*: At 30 mth. thenars 3; recovery of sensibility, no over-reaction, localization fairly good, two-point discrimination 15–20 mm.
C.113	Jan., 1944	Upper arm	9	Nov., 1944	10	8·2	21 above	++	C.S. ulnar	Large gaps; mobilization undesirable on account of scarring	*Recovering*: At 22 mth. P.T. and F.C.R. 3, F.D.S. 2; some return of pain sensibility
B.206	Feb., 1944	Forearm	10	Dec., 1945	22	7	16 below	+++	C.S. ulnar	Late operation; ulnar graft used, since suture of the ulnar lesion would have been valueless	*Probable failure*: At 13 mth. a little return of pain sensibility
B.159	May, 1944	Elbow	4	Dec., 1944	7	7	8 above	+++	C.S. ulnar	Separation of suture line	*Success*: At 21 mth. P.T. 4, F.C.R., F.D.S. 3·5, P.L., F.P.L. 3. Coarse touch and nearly normal pain sensibility, without over-reaction, in median area
W.104	June, 1944	Upper forearm	10	May, 1945	11	4·5	14 below	++	C.S. ulnar	Large gaps	*Success*: At 20 mth. no recovery in thenar muscles, which were very wasted. Pain and light touch felt everywhere; localization poor, very slight over-reaction
H.112	July, 1944	Arm	0	Nov., 1944	4	14·3	11·5 above	None	C.S. radial	Large gaps	*Recovering*: At 19 mth. P.T. F.D.S., F.D.P. 4, F.C.R. 3, F.P.L. 2. Partial return of pain sensibility
W.121	July, 1944	Axilla	5	March, 1945	8	7	22 above	+	C.S. musculocutaneous C.S. medial cutaneous	Mobilization undesirable on account of vascular injury; donor nerves irreparable	*Partial Recovery*: At 22 mth. feeble power in long flexors, but touch and pain felt throughout
D.59	Sept., 1944	Arm	11	Oct., 1945	13	11	16 above	++++	C.S. ulnar	Mobilization impossible on account of scarring; large gaps	*Probable failure*: At 12 mth. no clear evidence of recovery
H.142	May, 1945	Axilla	4	Oct., 1945	5	15	29 above	+	P.S. ulnar, two strands	Large gaps	*Too early for assessment*, but recovery is commencing

To face page 160

Table VI.—GROUP C: MAIN-TRUNK GRAFTS (VARIOUS NERVES)

NUMBER	DATE OF INJURY	NERVE	INTERVAL BEFORE HEALING (MONTHS)	DATE OF GRAFTING OPERATION	INTERVAL BETWEEN INJURY AND REPAIR (MONTHS)	EXTENT OF GAP (CM.)	LEVEL OF UPPER SUTURE LINE	SCARRING	DONOR NERVE (C.S., Central Stump P.S., Peripheral Stump)	REASON FOR GRAFTING OPERATION	RESULT
A.35	May, 1943	Medial popliteal	4	Dec., 1943	7	10	21·5 cm. above knee	++	Two strands of lateral popliteal, one central, one peripheral	Separation of suture	*Partial recovery*: Calf muscle 3½ at 39 mth.
W.80	July, 1943	Medial popliteal	11	Nov., 1944	16	12	41 cm. above knee	++++	Two strands of lateral popliteal, P.S.	Large gap, stiff knee	*Probable failure*, though the lesion was a high one. No recovery at 22 mth.
S.113	Nov., 1943	Medial popliteal	5	Oct., 1944	11	11·3	48 cm. above knee	+++	Two strands of lateral popliteal, P.S.	Large gap	*Failure*: No recovery at 22 mth.
B.185	June, 1944	Sciatic	10	Oct., 1945	16	16	34 cm. above knee	+	Main sciatic trunk from other side—below-knee amputation	Large gap	*Too early for assessment*
B.198	Jan., 1945	Medial popliteal	1	Oct., 1945	9	5·5	16·5 cm. above knee	0	Two strands of lateral popliteal, C.S.	Large gap	*Probable failure*: No useful recovery at 16 mth.
H.58	Nov., 1942	Cervical 5 (6·7)	0	Aug., 1943	9	9·5	Transverse process of C.5	+	Radial, P.S.	End-to-end suture impossible	*Failure*
D.48	Dec., 1943	Musculo-cutaneous	2	April, 1944	5	7·5	3·5 cm. below coracoid	+	One strand of normal medial cutaneous	Large gap	*Success*: Power in biceps returning after 9 mth., and 4½ after 20 mth.
J.33	June, 1943	Medial plantar	6	March, 1944	8	3	2 cm. below malleolus	++	Lateral plantar, C.S.	Alternative (probably better) would have been mobilization of the posterior tibial nerve to the knee	*Failure*
W.73	March, 1943	Deep (motor) branch of ulnar	4½	Sept., 1943	6	4	Pisiform	++	Degenerate dorsal cutaneous branch of ulnar	End-to-end suture impossible	*Failure*: Possible on account of atrophy and ischæmia of interossei

Table VII.—GROUP D: PARTIAL LESIONS: INLAY GRAFTS

NUMBER	DATE OF INJURY	NERVE	LEVEL	INTERVAL BEFORE HEALING (MONTHS)	DATE OF GRAFTING OPERATION	INTERVAL BETWEEN INJURY AND REPAIR (MONTHS)	EXTENT OF GAP (CM.)	LEVEL OF UPPER SUTURE LINE	SCARRING	DONOR NERVE	RESULT
E.1	Nov., 1940	Two-thirds of trunk of C.5 and 6	Posterior triangle of neck	0	May, 1941	6	5·5	Transverse processes	0	Three strands of normal superficial radial	*Success*: At 36 mth., deltoid 3, biceps 4, and almost complete sensory recovery
B.93	April, 1943	Posteromedial, presumably sensory, half of median	Lower arm	5	Dec., 1943	8	5	10 cm. above elbow	0	One strand of normal medial cutaneous	*Success*: At 38 mth., all muscles working at 4–5; hypoæsthesia and hypoalgesia at finger-tips. No over-reaction
J.49	June, 1944	Posterolateral half of ulnar	Upper arm	1	Aug., 1944	1½	2·6	20 cm. above elbow	0	One strand of normal medial cutaneous	*Success*: At 26 mth., all muscles except one, 4+, with good independent movement. Slight hyperalgesia. Two-point discrimination 8 mm. (normal 3)
G.78	July, 1944	Superficial half of median	Upper arm	2	Nov., 1944	4	3	23 cm. above elbow	+	Two strands of normal medial cutaneous	Patient could not be traced after one year
S.155	Aug., 1944	Posteromedial half of ulnar	Upper arm	¾	Feb., 1945	6	3	23·5 cm. above elbow	0	One strand of normal medial cutaneous	No conclusive evidence of recovery at 14 mth., but lesion was high one. Follow-up now impossible as patient has gone abroad
S.158	Feb., 1945	Cervical 5, C.6 in continuity and apparently healthy	Posterior triangle of neck	¾	April, 1945	2	3 4·5 5	Transverse process	+	Three strands of normal medial cutaneous, each going to separate bundle below	No conclusive evidence of recovery at 21 mth.
O.18	Feb., 1945	Posterolateral half of ulnar	Arm	2	July, 1945	5	1·5	6·5 cm. above elbow	+	Two strands of normal medial cutaneous	*Blind*: Unable to attend for examination.

OPERATIONS.—

Oct. 25: *Exploration of left radial nerve.* The nerve was found to be completely divided with a gap of 9 cm. between the stumps. Resection would have increased the gap to at least 11 cm., so repair of the nerve was not attempted. The elbow-joint could not be flexed beyond 90°, and even anterior transposition of the nerve would not have permitted closure of the gap. Bone shortening was a possibility, but it was decided to postpone such a radical step until the time when the median nerve was explored.

Nov. 20.: *Exploration of the median, musculocutaneous, and ulnar nerves,* through an incision extending from the coracoid process to just above the elbow-joint.

Ulnar nerve: this was not explored, since by this time good power was returning.

Sept. 12, 1945: *Arthrodesis of the wrist* by Smith-Petersen's method and transplantation of flexor carpi ulnaris, which was now strong (4/5 M.R.C. grading), into the extensors of the digits. By this time there was an encouraging return of power in the biceps (2½), so the question of repair of the musculocutaneous nerve no longer required consideration.

PROGRESS.—

June 15, 1946: Arthrodesis of the wrist sound, transplant working satisfactorily. The ulnar intrinsic muscles were working well (3½). All muscles innervated by the median nerve were active except the thenars; good flexion of the fingers (4).

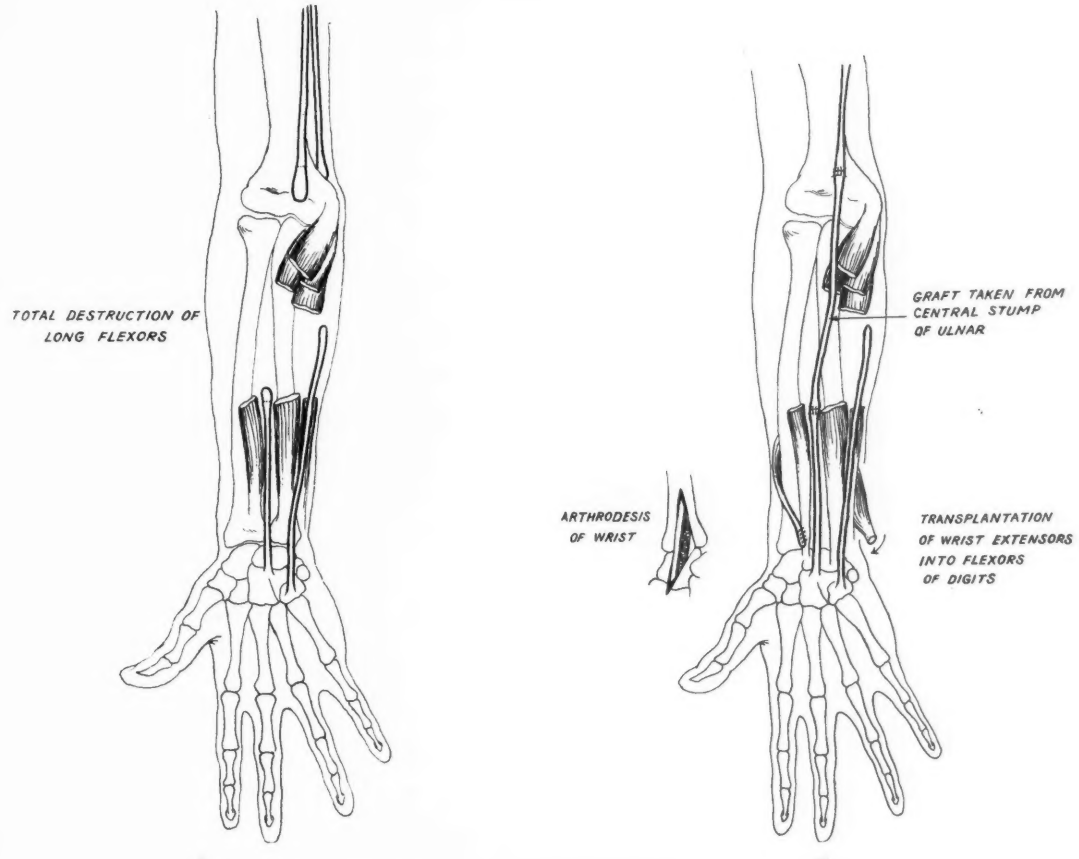


FIG. 163.—A, Large gaps in the median and ulnar nerves: destruction of long flexors; B, Median repaired with graft taken from central stump of ulnar. N.B.: The upper suture line should have been drawn at a rather lower level (S.63, *Table V*).

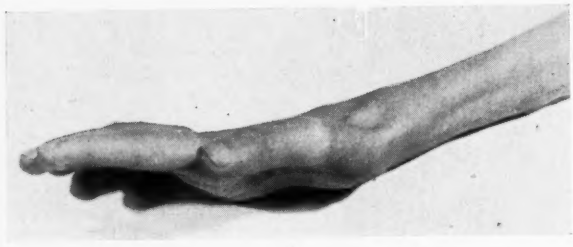
Musculocutaneous nerve: there was a severe traction lesion just proximal to the point of entry of the nerve into coracobrachialis, with a firm neuroma 1·5 cm. long. Since the nerve appeared to be in continuity no repair was attempted, although electrical stimulation was negative.

Median nerve: there was a most remarkable traction lesion, with a firm lobulated neuroma, 3·3 cm. long, just below the junction of the two heads of the median nerve, a gap of 4·6 cm., and a peripheral stump which was extremely attenuated over a length of 4 cm. It was estimated that the gap after adequate resection would be about 14 cm., and it was therefore decided to use the proximal stump of the radial nerve as a graft to bridge the gap in the median. The gap was in fact exactly 14 cm., and a satisfactory repair was effected (*Fig.* 162).

Jan. 8, 1947: Coarse touch and pain sensibility present in median area.

On Nov. 4, 1942, S.63, a mechanic, suffered a deep laceration extending from the elbow to the lower third of the forearm, with complete median and ulnar paralysis; no fracture. Excision of the wound was performed five hours after injury; there was almost complete destruction of the flexor mass and large gaps in the median and ulnar nerves; the medial humeral epicondyle was comminuted and the elbow-joint open. After excision of all damaged and devitalized tissue the nerve stumps were anchored where they lay, the upper end of the wound was closed by the application of a split skin-graft, and the limb was enclosed in plaster-of-Paris. Healing was uneventful; later the scar was replaced by a flap-graft from the abdominal wall.

July 14, 1943: *The median and ulnar nerves were explored.* Since after resection of the end-bulbs the gap in the median was 13 cm. it was decided to close it with a graft from the central stump of the ulnar nerve (*Fig.* 163). There was, of course, complete paralysis of the long flexors of the fingers and thumb due to direct damage to the muscles, and it was therefore decided to await the result of the nerve-grafting operation before taking steps to make good this deficiency.



A

FIG. 164.—*Case* S.63 (*see Fig.* 163). Result of arthrodesis of wrist, followed by transplantation of wrist extensors into flexors of digits.

By early June, 1944, there were unmistakable signs of returning sensibility in the median area, and an arthrodesis of the wrist was therefore performed by Smith-Petersen's method. This permitted the subsequent borrowing of the extensors of the wrist (E.C.U., E.C.R.L. and B.) for transplantation into the flexors of the digits, and this second operation was performed on Sept. 20, 1944.

By July, 1945, the return of function in the hand was remarkable. The thenar muscles were strong (4); there was return of touch and pain sensibility to the finger-tips, though localization was poor; and a powerful though limited range of flexion of the fingers (*Fig.* 164).

In 8 of the 13 cases of median nerve injury treated by main-trunk grafting there was division of the large blood-vessels. In 4 loss of skin was such

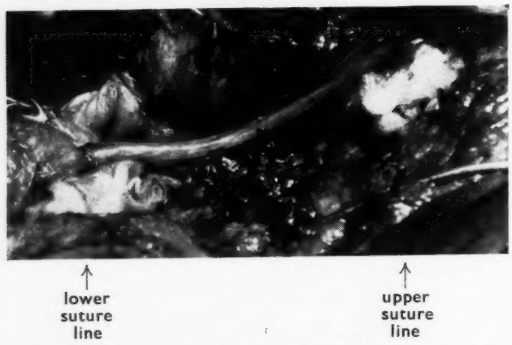
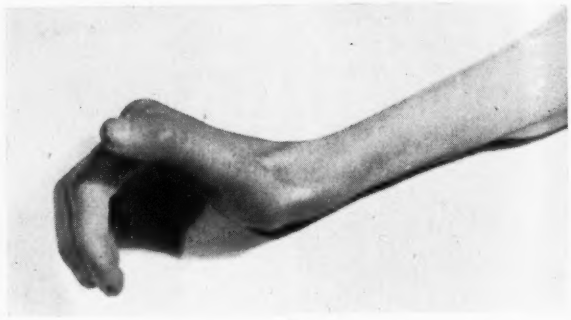


FIG. 165.—Large gap in the medial popliteal division of the sciatic nerve repaired with two strands from the lateral popliteal.

as to require plastic repair, and in 8 cases there was an irreparable lesion of the ulnar nerve, which was the reason for the employment of this nerve as a graft for the median. It is remarkable that such a high proportion of successes was obtained in view of the generally unfavourable nature of these injuries.

In 4 cases of sciatic nerve injury two strands of the lateral popliteal nerve were used as a graft for repair of the medial (*Fig.* 165). In all but 1 of these 4 cases conditions were uniformly unfavourable and in only one has useful recovery yet been observed.

In another case of sciatic nerve injury with a large gap a main-trunk sciatic graft taken from the other limb, which had been amputated below the knee, was used to bridge the gap (*Fig.* 166). H.58, the brachial plexus lesion was due to traction. Unfortunately, resection was inadequate, though the procedure used probably has a place in the surgery of brachial plexus injuries. In a lesion of C.5, 6,



B

and 7, with the complete paralysis of all muscles supplied by the radial nerve, the peripheral stump of the latter was used for the repair of C.5, the central stump of C.6 being so unsatisfactory as to preclude all possibility of successful repair.

The last 3 cases in Group C differ from the rest in that the nerves involved were of comparatively

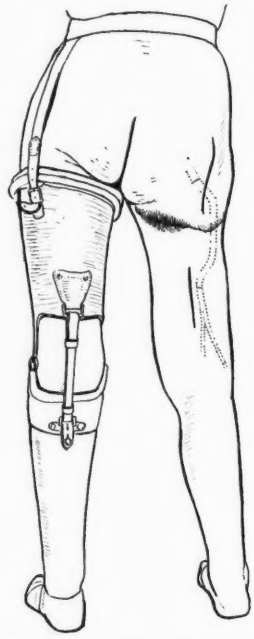


FIG. 166.—A by-pass operation, in which a segment of the left sciatic trunk was used for repair of a very large defect in the right. A below-knee amputation had been performed on the left (B.185, *Table VI*).

small diameter. The case of division of the musculocutaneous nerve with a large gap was a striking success; recovery in the biceps, though not in brachialis, was little short of complete. The attempt to repair the medial plantar nerve by using the central stump of the lateral plantar was an

ill-conceived experiment. Subsequent experience has convinced us that the proper remedy in cases where limited mobilization is insufficient for end-to-end suture of a low lesion of the posterior tibial nerve, is mobilization of the nerve to the knee. This procedure is less formidable than it sounds and can be accomplished with little disturbance of the gastrocnemius or soleus muscles. The attempt to repair a lesion of the deep branch of the ulnar nerve was frustrated by irreversible atrophy of the interossei.

Group D: Inlay Graft for the Repair of Partial Division of a Nerve (*See Table VII*).—After repairing a partially divided nerve the assessment of recovery must be made with unusual caution, since one is concerned not with recovery as compared with complete paralysis, but with different degrees of function—that mediated by the undamaged part of the nerve compared with the sum total mediated by the nerve, after repair of the damaged part by grafting. In the case illustrated in *Fig.* 159 (J.49, *Table VII*), the lesion was about 48 cm. proximal to the wrist, and no recovery occurring within less than about 500 days after operation could possibly have been due to the operative repair; the operation was performed on Aug. 9, 1944, and the significant developments were those occurring after Dec. 31, 1945. There was a very striking improvement during 1946. With the exception of the first dorsal interosseous ($3\frac{1}{2}$) all the ulnar muscles worked at $4\frac{1}{2}/5$, with excellent independent movement. The restoration of sensibility was equally gratifying, two-point discrimination on the pulp of the little finger being 8 mm. compared with 3 mm. on the normal side.

Although our experience of repair of partial lesions by inlay grafting is very limited, the collateral evidence provided by cases in which the whole thickness of a nerve has been repaired by grafting is so favourable that one has no hesitation in recommending a procedure so technically unexceptionable. If a complete lesion can be repaired by grafting, then *a fortiori* a partial lesion may be dealt with in the same manner.

DISCUSSION

It has previously been demonstrated beyond all reasonable doubt that autogenous nerve-grafting is satisfactory under experimental conditions and, in clinical practice, for the repair for small nerves such as the facial or the digital nerves of the hand.

Furthermore, reports of partial or complete success in the repair of major nerve-trunks in the limbs have not been wholly lacking—Medical Research Council 1920, 1942; Bunnell and Boyes, 1939; Klar, 1943. In this paper an attempt has been made to show that good results may be obtained with some regularity.

Between January, 1941, and June, 1946, a period of five and a half years, 59 cases of peripheral nerve injury in the limbs have been dealt with by means of autogenous grafting at the Oxford Peripheral Nerve Injuries Centre. Only one of these cases has been excluded from this report, the reason being that the patient was killed in an accident seven months after his operation, and it was therefore impossible to assess the result. Fifty-two of the 58 cases have been followed for a sufficient length of time to permit a reliable assessment of the results (*Table VIII*). In 20 (38·5 per cent) recovery was as good as that seen after the most satisfactory end-to-end suture of the same nerve injured at the same level. In a further 7 cases recovery is proceeding so satisfactorily that it is not unreasonable to anticipate that it will ultimately be as good as in the first 20; thus the possible total of good results is 27—51·9 per cent. In a further 8 cases there has been partial recovery which, although disappointing, is not altogether valueless; hence the operation has yielded a useful return in no less than 35 out of 52 cases—67·3 per cent. The cases that appear in the tables as 'probable failures' are here (*Table VIII*) added to the undoubted failures, bringing the total to 17 or 32·7 per cent of the total. When it is remembered that most of the cases in which nerve-grafting was performed had suffered exceptionally severe injury, this record of success is impressive; it establishes autogenous grafting as a worth-while and reliable procedure in peripheral nerve surgery.

When a reasonable measure of success is claimed for a procedure which in the hands of other surgeons has produced indifferent or frankly unsatisfactory results, the whole situation calls for the most searching review. The claimant must satisfy himself and others that there has been no element of self-deception in the assessment of results. In following up our cases of nerve-grafting exactly the same criteria of recovery have been used as in cases of end-to-end suture, the precise methods of examination accepted by the Medical Research Council and all the Peripheral Nerve Injury Centres in Great Britain being employed; furthermore, every case has been examined independently by two, and most of them by three, observers, who have checked each other's findings with severe impartiality. The results of these examinations have been set out at length, and although they make tedious reading no apology is made for their inclusion, for other workers must have access to evidence on which they may base their own judgements.

It is equally necessary to determine the factors essential to success, for only in this way can the operation of nerve-grafting become established as a reliable procedure, one that can be counted on to give a fair proportion of satisfactory results in the hands of any competent surgeon. If nerve-grafting is considered in comparison with the grafting of two other kinds of tissue, bone and skin, now both commonplace procedures, the most striking difference that emerges is that in the case of peripheral nerve tissue there is no margin for technical error. In the case of grafting skin or bone unfavourable factors such as faulty apposition or moderate sepsis may mar the result, though not necessarily irretrievably; what has been lost may be only a small proportion of the whole and the defect may be made good subsequently. On the other hand one single unfavourable factor or one technical mishap is enough to ruin a nerve-graft beyond hope of redemption; the whole mechanism of nerve regeneration is one of such great delicacy.

Success depends on the observance of the following points, the first four of which are of equal importance in repair of a nerve by end-to-end suture:—

a. The interval between injury and repair should be as short as possible. From the moment of injury

there is a progressively harmful shrinkage of the Schwann tubes in the peripheral stump of the nerve (Holmes and Young, 1942; Sanders and Young, 1944); an even more injurious progressive atrophy of denervated muscle, with interstitial fibrosis and disappearance of motor end-plates (Gutmann and Young, 1944; Bowden and Gutmann, 1944); and similar though less well understood changes in sensory end-organs and other tissues. Although there is a good prospect of repairing a nerve successfully at any time up to one year after injury, there is little doubt that the sooner repair is carried out the better, and with this in view all possible steps should be taken to obtain early healing of wounds or union of a fracture.

b. We have seen a few cases in which sutured nerves came apart as a result of sepsis and if a graft is used for repair of a nerve the possibility of its death, should sepsis intervene, is an added hazard. We have, therefore, always postponed operation until sound healing of the original wound has occurred and protective chemotherapy was always employed. Sepsis was avoided in all cases.

c. Resection of the nerve stumps must be adequate. There is no difficulty with the central stump (except in the case of a traction lesion, where the central damage is always considerable) but, as has already been shown, there is a considerable risk of inadequate resection of the peripheral stump. The peripheral resection should be generous, especially in the case of digital nerves, in order to get back to bundles that have not become collagenized as a result of ischæmia. In every case the state of the nerve stump should be checked histologically.

Table VIII.—Summary of Results

	Recovery	Recovering	Partial Recovery	Failure	Too Early to Assess	Total
A. Digital	5	2	3	6	—	16
B. Cable :—						
Median	3	2	—	1	—	6
Brachial plexus	—	—	1	2	—	3
Others	1	1	2	—	—	4
C. Main Trunk :—						
Median	7	2	1	2	1	13
Sciatic	—	—	1	3	1	5
Others	1	—	—	3	—	4
D. Inlay for Partial Division	3	—	—	—	4	7
	20	7	8	17	6	58

Table IX.—Causes of Failure

Case		Undue Delay (Extreme Muscle Atrophy)	Inadequate Resection (Traction Lesion)	Ischæmia of Peripheral Stump	Predegenerate Graft	Great Scarring of Bed for Graft	Ischæmia of Graft	No Known Reason
Table III Digital Nerve-grafts	Mc.1			+				
	C.19			+				
	A.12			+				
	S.27							+
	N.13 (part only)				+			
	M.96			+				
	K.30							+
Table IV Cable Grafts	B.27		+					
	A.17	+	? +					
	R.75			+				
	B.146a			+				
Tables V and VI Main-trunk Grafts	B.206	+						
	D.59					+		
	A.35						+	
	W.80	+			+	+	+	
	S.113				+	+	+	
	B.198						+	
	H.58				+			
	J.33							+
	W.73	? +						
		3–4	1–2	6	3–4	3	4	3

d. The preservation of a healthy condition of the joints, muscles, tendons, and skin must be such that restoration of function will be satisfactory should adequate regeneration follow repair of the nerve. Provided that it has not led to frank ischæmia of the peripheral muscles damage to a main blood-vessel seems to have had surprisingly little harmful effect on the progress of recovery; repair of a nerve either by end-to-end suture or by grafting should not be withheld simply because there has been division of, say, the axillary or brachial artery.

Other factors are peculiar to nerve-grafting and, naturally, are chiefly concerned with the graft itself.

e. The graft must be rather longer than the gap to be bridged so as to make allowance for shrinkage. If a graft of exactly the same length as the gap is

employed there is a risk of separation at one suture line. It has been suggested by Klar (1943) that a graft is not likely to be successful if its length exceeds 6 cm.; this is not borne out by our experience. Cutaneous nerve-grafts (*Table III* and *IV*), of 7, 10, and even 12 cm. have been employed with success; a number of successes (*Table V*) have also been recorded after the implantation of main-trunk grafts of 8, 12, and even 14·3 cm. The results after bridging large gaps are as good as those in which only short grafts have been used.

f. The main-trunk graft or cable graft made up of strands of cutaneous nerve must have a cross-section area at least equal to the diameter of the peripheral stump; otherwise there will not be a sufficient number of channels to ensure adequate re-innervation. Unfortunately the employment of a graft taken from a nerve-trunk of considerable diameter introduces another risk of failure—necrosis or collagenization of the graft from ischæmia. In four cases of sciatic nerve injury (*Table VI*) the medial popliteal component was repaired by the implantation of two strands taken from the lateral popliteal. In a fifth case a segment of normal sciatic nerve from the other side (on which amputation through the leg had been performed) was used for repair of an enormous gap in the sciatic nerve. In this last case it is as yet too early to make a definite assessment of the result, but in the other four partial recovery occurred only in one. In two, W.80 and S.113, conditions were exceedingly unfavourable; the operations were formed late, there had been extensive sepsis, and the whole zone of operation was converted into scar tissue. In the other two, A.35 and B.194, conditions were moderately favourable. This record of failure is such that one must make the working assumption that the lateral popliteal nerve, when used as a free graft, is, on account of its size, liable to serious ischæmic changes. Some remedy must be found. Unless the gap is a short one cable grafting is out of the question, since in the case of the medial popliteal division of the sciatic nerve alone it would hardly be possible to obtain an adequate supply of material from cutaneous nerves. It is possible that Strange's (1947) pedicle-grafting technique will prove the solution to this problem.

g. Such evidence as is available suggests that it is wiser to use normal nerve as graft material rather than part of the peripheral stump of a divided nerve that has been degenerate for many months; in cases where the latter has been used the results have been disappointing. However, in *Case* A.35, referred to above, a biopsy taken from the piece of the central stump of the lateral popliteal nerve that had been used as a graft showed necrosis, whereas the specimen taken from the degenerate graft, which came from the peripheral stump of the same lateral popliteal nerve, showed some degree of re-innervation and and no necrosis. Thus a free graft from the central stump of a very large nerve may be even less satisfactory than one from the peripheral stump. There are a number of interesting questions concerning the survival of different kinds of grafts which still await solution.

h. The bed in which the graft lies is of importance in determining its survival, especially in the early days before satisfactory vascular connexions have been made with the central and peripheral stumps. If possible all scar tissue should be removed; if this cannot be done then the graft should be led through a tunnel of healthy tissue, by-passing the zone of cicatrization. For the same reason all wrapping materials should be avoided, and if plasma is used for fixation of the grafts it should be applied only at the junctions and not throughout their length. Hæmostasis should be complete so that the graft will not be separated from its bed by an effusion of blood.

i. Suture. It is almost platitudinous to observe that all the effort expended in dissecting out the stumps of a badly damaged nerve and preparing them for repair is thrown away if the last and crucial step in the operation, whether it be end-to-end suture or the implantation of a graft, is not technically perfect. Yet sometimes the surgeon, after a long and exacting dissection perhaps not free from anxiety if he has been working in the neighbourhood of large blood-vessels, comes to this final step with his vision a little dimmed and his hands no longer completely steady. Unless he is still feeling fresh and confident of his dexterity it is best for him, even at the risk of being considered fussy, to leave the theatre for a few minutes and relax before completing the operation; or he may ask a colleague if one happens to be available, to perform the suture. Delicacy of touch often deteriorates after two or three hours' continuous operating, and in these particular operations is at its lowest ebb at the time when it is needed most. Fortunately, where cutaneous nerve-grafts are used—and they were formerly the most difficult of all to handle—suture has been greatly simplified by the introduction of concentrated plasma, though considerable skill is still necessary in maintaining precise apposition of the grafts with the nerve stump before and during the application of the fibrinogen solution. But at all costs the suture must be as nearly perfect as possible.

The operations described in this paper have been done by three people, by the writer and by his two assistants, Mr. R. B. Zachary and Miss R. E. M. Bowden. The results bear no relation to the individuals concerned, and provided that due consideration is paid to all the factors that have been enumerated autogenous nerve-grafting may be relied upon to yield satisfactory results.

The causes of failure (*Table IX*) are instructive and emphasize the importance of the several factors that have just been discussed.

N.13 is here included among the failures (the case appears elsewhere as a partial recovery) because two of four digital nerve-grafts employed were degenerate; no recovery occurred in the zone supplied by the nerves concerned, whereas good sensibility returned in the zone supplied by the other two branches repaired by the implantation of grafts taken from normal cutaneous nerve.

In some cases more than one factor might have been responsible for failure. To steer a safe course between all these obstacles obviously calls for considerable judgement, but in the light of experience gained as a result of this investigation it should be possible more often than not.

SUMMARY

Analysis of 1681 cases of nerve injury showed that 699 (41·5 per cent) required operative repair. End-to-end suture was performed in 71 per cent, bulb suture in 0·4 per cent, and suture with bone shortening in 0·4 per cent. Autogenous nerve-grafting was carried out in 8·6 per cent (59 cases), and in 19·5 per cent the lesion was too extensive for any kind of operative repair. Since it has been shown that the closure of large gaps by end-to-end suture is undesirable, on account of the damage inflicted on the shortened nerve when the acutely flexed limb is extended, it is probable that a rather greater proportion of the total number of cases requiring radical repair ought to be dealt with by other means, if such is available. Thus, if autogenous nerve-grafting is shown to be a reliable procedure, the field for its application may be not inconsiderable.

There is no reliable evidence that heterogenous and homogenous nerve-grafts are of the slightest use in clinical practice; autogenous nerve-grafting alone offers any prospect of success.

In a series of 58 cases in which extensive gaps have been repaired by the implantation of autogenous grafts 52 have been followed for a sufficient length of time to permit a fair assessment of the efficacy of the operation. In 20 (38·5 per cent) recovery was as good as that seen after the most satisfactory end-to-end suture of the same nerve injured at the same level. In a further 7 cases recovery is proceeding so satisfactorily that it will almost certainly be as good as in the first 20; thus the possible total of good results is 27—51·9 per cent. Partial but useful recovery has occurred in 8 cases; the operation was, therefore, of value in no less than 35 out of 52 cases—67·3 per cent.

There can be few procedures in which success is more dependent on the proper management of the case from first to last. As in end-to-end suture, it is desirable to repair the nerve as soon as possible, and healing of the primary wound must be hastened by every available means. The denervated part must also be maintained in good condition.

After nerve injuries of great severity—and it is in such cases that grafting is particularly necessary—there may be unusually extensive collagenization of the peripheral stump, resection of which should, therefore, err on the side of generosity.

Grafts may be taken from any cutaneous nerve, though only from the part in which no branches are given off. The most suitable are the medial cutaneous nerve of the forearm, where it lies in the arm; the sural proximal to the lateral malleolus; the superficial radial proximal to the wrist; and the saphenous in the thigh. Single strands are used for the repair of small nerves such as the digital; two to four strands may be employed for bridging gaps in larger nerves.

Where two main trunks have been very extensively damaged a segment from the less important may be used for the repair of the gap in the more important nerve. In three cases presenting unusual features a half segment of the median was used for repair of the other half. An attempt was also made to repair the medial popliteal by using two strands from the lateral popliteal component of the sciatic nerve. In one case the whole thickness of the sciatic trunk, taken from the other side where a below-knee amputation had been performed, was used for repair of both divisions of the sciatic. There is a risk of central necrosis or of excessive collagenization in a graft taken from a nerve-trunk of considerable diameter; the ulnar and radial nerve-trunks have been employed with success, but not the lateral popliteal or the whole sciatic trunk. It is probable that the latter exceeded the critical diameter.

Long-standing degeneration, as in a graft taken from the peripheral stump of a nerve divided at the time of the original injury, seems to be harmful; a graft of the thickness of the lateral popliteal nerve is less likely to become ischæmic if it comes from the peripheral stump.

All grafts shrink; the graft or collection of grafts should, therefore, be about 15 per cent longer than the gap to be repaired; otherwise separation at one suture line may occur.

The diameter of the graft or collection of grafts must be at least equal to that of the peripheral stump of the nerve that is being repaired.

A graft is revascularized from the nerve stumps to which it is sutured but is also nourished to some extent—and this is of great importance if the length of the graft is considerable—from the bed in which it lies. Scar tissue should, therefore, be removed as widely as possible; if a satisfactory bed cannot be obtained in this way the graft should be led through a by-pass traversing healthy tissue.

The scope of the grafting operation may be greatly increased by shortening the gap to be closed by means of the standard technique of mobilization which is invariably employed in secondary suture. In this way it is sometimes possible to bridge gaps that could not otherwise be repaired with the limited amount of graft material that may reasonably be taken from other peripheral nerves.

Inlay grafting is the ideal treatment for partial division of a nerve.

Main-trunk grafts are sutured in the usual way to the stumps of the host nerve. Cutaneous grafts, whether used singly or in the form of a cable, are best attached with concentrated fibrinogen which can be made to set very rapidly into a firm clot.

The results of operation are reported in full.

Throughout this prolonged investigation, involving much detailed follow-up work, I have been most ably assisted by my junior colleagues, and am particularly indebted to Mr. R. B. Zachary and Miss R. E. M. Bowden. Mr. William Holmes was responsible for all the histological work, which is reported in the following paper; he has also been good enough to read this paper and to make a number of valuable suggestions for its improvement.

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HISTOLOGICAL OBSERVATIONS ON THE REPAIR OF NERVES BY AUTOGRAFTS

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THE results of autogenous nerve-grafting, as demonstrated by the Oxford series of cases, is reported by Seddon in the previous pages. This paper is based on an investigation of the same series, and is concerned with two important practical aspects of the problem, as illuminated by histological study. These are: first, the fate of ' full-thickness ' grafts (those taken from a main nerve-trunk); and, second, the effect on recovery of the condition of the endoneurium in the distal trunk of the recipient nerve.

I. THE FATE OF TRANSPLANTED NERVE-TRUNKS

A segment of normal nerve excised for the purpose of grafting elsewhere resembles the distal trunk of a divided nerve in that its axons are separated from their cell bodies: Wallerian degeneration will therefore take place within the graft. But it differs from a distal trunk in that it is divided at two levels and is removed from its bed; it is, therefore, wholly deprived of its blood-supply. This devascularization may well be feared to cause irreparable damage, and the suspicion that it does so is sufficient to account for the almost complete avoidance of main-trunk grafts in clinical practice. The revascularization of a graft takes place both from the two ends of the host nerve and from adjacent tissues, but the process may not be quick enough to avoid abnormal metabolism and even death of the constituent cells in the middle of a thick transplant. The thinner units of cable grafts, on the other hand, are likely to be more rapidly revascularized and such grafts have enjoyed a limited popularity.

Nevertheless the clinical reports show that main-trunk grafts are sometimes successful (Seddon, 1947). Consequently it seemed that histological study of transplanting nerve-trunks in man could not fail to help in determining the possibilities and limitations of grafts of this type. The ideal method for such a study would be that of examining a graft that had been attached for some time to the stumps of the host nerve. But such a procedure is seldom justified, and we ourselves have had to be content with two cases, in which superficial biopsies were taken from a graft. The manner in which nerve biopsies are taken and examined is described by Holmes and Zachary (1946). The other observations were made on experimental transplants: segments of nerve excised and transplanted at the conclusion of an exploratory operation, and removed later for histological examination when a second operation—tendon transplantation—was performed.

BIOPSY OF NERVE-GRAFTS

Case A.35.—

May 1, 1943: A shell wound of the thigh divided the sciatic nerve.

Oct. 16: End-to-end suture was performed; gold plates were attached to the nerve immediately above and below the suture line. Post-operative radiographs showed that the suture line had separated; there was no technical hitch either during or after the operation and the reason for the separation was unknown.

Dec. 2: The site of suture was re-explored and the medial popliteal division repaired, this time by an autograft. This was made up of two lengths of the lateral popliteal nerve, one from its proximal and one from its distal stump. The length of the grafts was 12 cm.; that from the central stump had a diameter of 8 × 4 mm. and that from the peripheral 7 × 4 mm.

April 16, 1945: Electromyograph. No evidence of re-innervation of the gastrocnemius.

April 18: Exploration of the grafts. Both suture lines were intact, but adherent to the surrounding tissues.

The nerve above and below was easily separated, but the graft itself was more difficult to isolate, and numerous vessels ran into it from the soft-tissue bed. The length of the grafts was 10·5 cm.; the diameter of the inner graft (original distal stump) was 4 × 3 mm., that of the outer (original proximal stump) was 6·5 × 3·5 mm. Both felt firmer than normal. Biopsies were taken from the surfaces of the grafts: one from the inner, 6 cm. below the proximal suture line, and one from the outer graft, 2 cm. below the suture line. A further biopsy was taken from the distal trunk of the host nerve at a point 2·5 cm. below the distal suture line.

March 24, 1947: Power in calf muscle three-fifths normal.

The biopsy from the inner trunk of the graft presented a most encouraging appearance. There was some adventitious scar, but the sections contained several nerve-bundles which were completely innervated by regenerating nerve axons (*Fig.* 167). Many of these axons were of a diameter approaching that of large normal nerve-fibres and this shows that an autogenous graft from a distal trunk can serve as a satisfactory pathway for regeneration. In this case the nerve had been degenerate for seven months before use, but it had nevertheless been satisfactorily re-innervated, at least to a point 6 cm. below the proximal suture line.

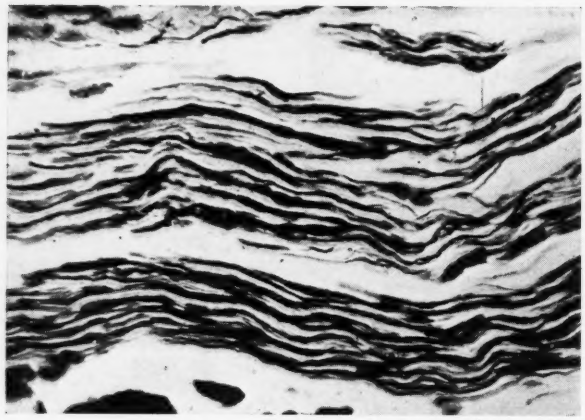

FIG. 167.—*Case A.*35. Biopsy from the distal stump graft. L. S. Axon stain. Full re-innervation. (× 560.)

The biopsy from the outer trunk, taken 2 cm. below the suture line, showed a much less satisfactory picture. The grafted nerve was a proximal stump containing normal nerve-fibres; the biopsy showed that these had failed to undergo normal Wallerian degeneration after grafting. The specimen contained four small nerve-bundles surrounded by dense scar tissue in which the collagen fibres were thick and sparsely nucleated. The inner structure of the bundles was characterized by the presence of large globules of fatty material, still staining with the hæmatoxylin of Weigert's method; these were undoubtedly the remains of normal nerve-fibres that had not been removed by the usual processes of Wallerian degeneration (*Fig.* 168). Correspondingly the endoneurial connective-tissue tubes around the fibre remains had retained their normal arrangement and had not undergone the collapse that characteristically accompanies Schwann-cell proliferation and fibre removal. Very few nuclei of any kind lay within the bundles. One small bundle, lying apart from the others, contained no myelin remains, but was occupied by a dense, sparsely nucleated mass of collagen. At no point in the nerve was there any evidence of regeneration, and the condition of the bundles can only be described as necrotic.

These findings are all the more remarkable in view of the fact that the specimen was taken from the surface of the graft, the part that should have had the best possible chance of being adequately revascularized from the surrounding tissues. The epineurium may perhaps have acted as a barrier since it is rather thicker in the sciatic nerve than in those of smaller diameter. The most significant factor was undoubtedly the dense scarring, which was widespread throughout the posterior part of the thigh.

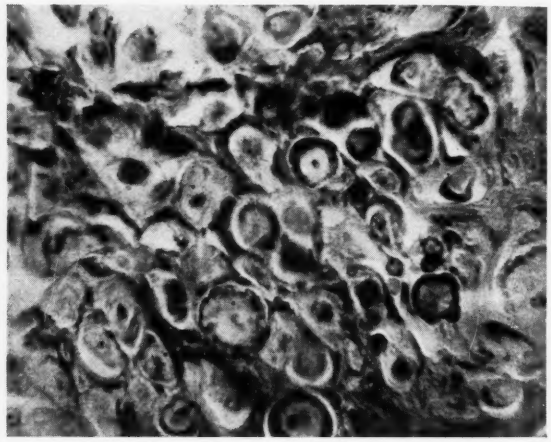

FIG. 168.—Same case. Biopsy from the proximal stump graft. T. S. Masson. Necrotic remains of normal nerve-fibres. (× 560.)

No attempt could be made to lead the grafts through healthy tissues.

The specimen from the distal trunk of the host nerve showed the normal appearance of Wallerian degeneration followed by sparse re-innervation: a few axons were visible at all points.

*Case S.*113.—

Nov. 6, 1943: Shell wound of the upper thigh divided the sciatic nerve.

Oct. 10, 1944: Nerve explored: gap after resection of stumps 11·3 cm. Medial popliteal division repaired with two grafts taken from the peripheral stump of the lateral popliteal.

Aug. 7, 1946: No sign of recovery. Grafts explored. Both of normal consistency, scarring around them not excessive. Biopsy specimen taken at a point 10 cm. below upper suture line: level of the latter 47·7 cm. above fibula.

March 10, 1947: Feeble flicker in calf muscle.

The specimen contained several small nerve-bundles, all of which were abundantly innervated by regenerating fibres: none of these had a total diameter greater than 4μ. There was no evidence of endoneurial abnormality or necrosis. The appearances were the same as those in the specimen taken from the peripheral stump graft in *Case* A.35, though in the latter some of the fibres were larger. So far as could be judged from the biopsy, good regeneration through the graft was taking place.

NERVE TRANSPLANTATION EXPERIMENTS

*Case B.*162.—This patient was found to have an irreparable lesion of the posterior interosseous nerve.

Oct. 18, 1944: At the conclusion of the exploratory operation the posterior interosseous nerve was divided at a level 3 cm. above the proximal end of the neuroma and immediately sutured back into its position; the distal end of this 'graft', i.e., the neuroma, was left free. The diameter of the graft was 3 × 2·5 mm.

Nov. 22: A tendon transplantation was performed. The graft was excised together with the suture line and part of the proximal stump above it.

Histological examination showed that the grafted nerve had undergone normal Wallerian degeneration. There was no evidence of abnormal fibrosis of the endoneurium nor of the interfascicular connective tissues; these seemed to be well vascularized and there was no evidence of necrosis or nuclear abnormalities (*Fig.* 169). The proximal end of the graft was abundantly innervated by regenerating nerve axons and many of these had traversed the whole length of it. This graft, 3 cm. × 3 mm. × 2·5 mm. had therefore behaved entirely normally during the first five weeks after suture.

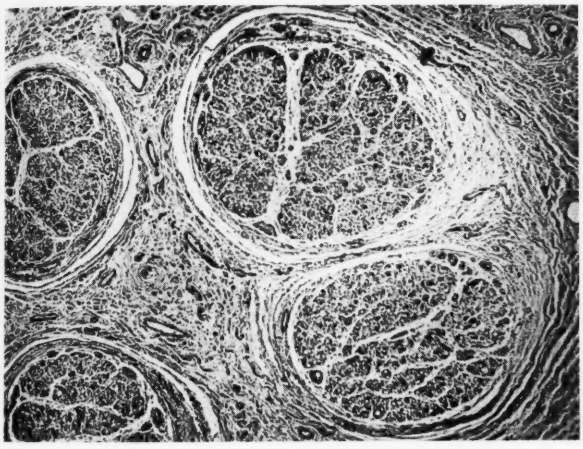

FIG. 169.—*Case* B.162. Nerve five weeks after transplantation. T. S. Masson. Bundles showing normal Wallerian degeneration. (× 48.)

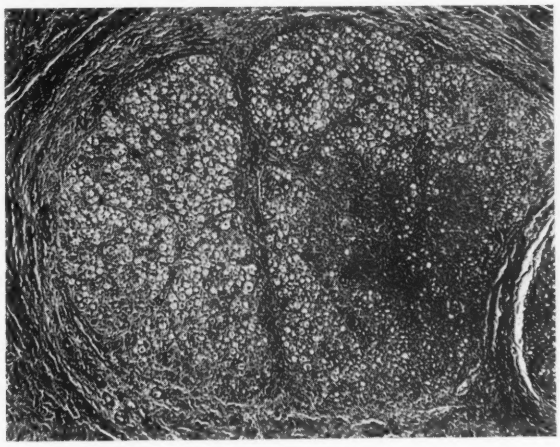

FIG. 170.—*Case E.*21. Nerve seven weeks after transplantation. T. S. Masson. Bundle showing delayed removal of myelin and, to the right, a patch of excess fibrosis. (× 48.)

*Case E.*21.—Irreparable radial nerve lesion.

Dec. 15, 1943: At the conclusion of the exploratory operation a portion of the proximal stump from above the neuroma, 7 cm. in length, was excised and transplanted to a position in the subcutaneous tissues. The transplant had a diameter of 6·5 × 3·5 mm.

Feb. 2, 1944: A tendon transplant was performed. The nerve transplant was excised: the diameter at its mid-point was 6 × 5 mm. and the centre had a slight yellowish tinge. The proximal and distal ends, which were white, were both swollen, having diameters of 8 × 11 mm. and 9 × 12 mm. respectively.

Histological examination showed that the swellings at the ends of the transplant were composed of fibrous tissue developed in relation to the suture material by which it was anchored into position. The epineurial connective tissue was increased in amount, but the increase was adventitious and not interfascicular; the connective tissue was not dense and appeared well vascularized. There was no inflammatory reaction. The nerve-bundles themselves varied in appearance at different levels in the specimen. In transverse section at the mid-point of its length there were several areas of nervous tissue in which Wallerian degeneration had not proceeded normally. There was marked local variation in the extent to which the Schwann tubes were collapsed and in the myelin remains removed. *Fig.* 170 shows one nerve-bundle in which, to the left, myelin remains are still seen occupying tubes having the diameter of normal fibres; to the right the myelin is all gone, and the tubes are collapsed so that their lumina are much finer, and there has been an increase of fibrous tissue in the endoneurium. In other areas the myelin had been removed and the tubes are collapsed, but there were local deficiencies of Schwann cells; at the periphery of the bundles the Schwann cells were for the most part present in normal numbers, while towards the centre they were extremely scarce. These abnormalities were present over a stretch of the nerve lying between points 8 mm. from each end; over the extreme proximal and distal 8 mm. degeneration had proceeded normally.

Within this transplant Wallerian degeneration had not proceeded normally; the abnormalities were most marked near the middle of the specimen along its longitudinal axis, and in the centres of the bundles on its transverse axis. It is true that, as a free transplant, it was deprived of the ingrowing blood-vessels that could be expected to penetrate it from the host stumps, but its collateral blood-supply could not be worse than that of a graft normally placed. Its length and diameter were greater than those of the graft described in the first experiment (*Case* B.162).

*Case R.*66.—Irreparable radial nerve lesion.

Jan. 24, 1945: At the conclusion of the exploratory operation a portion of the central stump of the radial nerve, 6 cm. in length, was excised and transplanted to a position in soft tissue. Its diameter was 5 × 5 mm.

April 18: A tendon transplantation was performed. Nerve transplant removed for histological examination.

The epineurial connective tissues were not significantly abnormal, and at all levels in the nerve contained small, new blood-vessels. There was no evidence of necrosis. At several points the perineurium of the bundles was somewhat changed, having lost its usual distinctness from the epineurium; when this was so the bundles appeared to 'merge' into the interfascicular tissues. Within the bundles there was no evidence of delayed removal of myelin remains, and the Schwann tubes were normally collapsed. But the endoneurial connective tissue showed a patchy abnormality. This is shown in *Fig.* 171; in the more lightly stained areas within

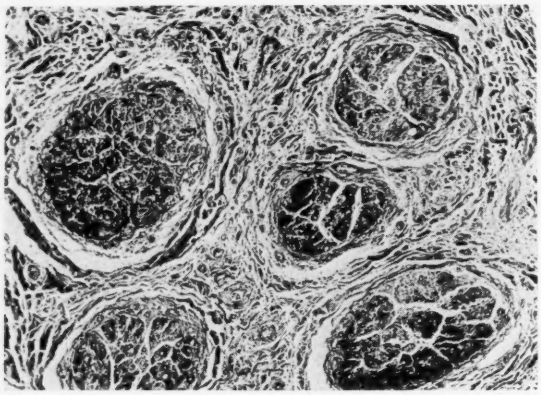

FIG. 171.—*Case R.*66. Nerve twelve weeks after transplantation. T. S. Masson. Bundles showing Wallerian degeneration, with darker patches indicating excess collagenization of the endoneurium. (× 48.)

the bundles the endoneurium is normal, but in the darker areas the collagen had increased unduly, so that the Schwann tubes were constricted by a thick collagenous matrix (*Fig.* 172). This endoneurial fibrosis is of a similar type to that discussed in the second section of this paper, where illustrations are also given of the normal appearance of Schwann tubes after Wallerian degeneration.

The condition of this transplant, twelve weeks after its transposition, was such that it would have been a fairly satisfactory nerve bridge, though the abnormality of the endoneurium might have impaired the quality of recovery.

DISCUSSION

The evidence presented above shows that grafts of the dimensions here used offer considerable prospects of success. All the abnormalities found are the result of interference with the normal course of Wallerian degeneration, and may be presumed to depend on the factor of revascularization. When a nerve is divided the Schwann cells are immediately stimulated into proliferation, and immigrating phagocytic cells remove the myelin and axon remains. Both types of cell are abnormally active and have, therefore, abnormally high metabolic requirements—just at the moment when the nerve is wholly deprived of its blood-supply. Hence it is not surprising that degeneration proceeds atypically. The evidence from the cases of nerve biopsy, where the predegenerated grafts were successfully innervated while the proximal stump graft was necrotic, emphasizes an important possibility. The cells in a nerve-trunk are at the height of their activity during a period of some three weeks after section of the nerve; thereafter they return to relative inactivity and their metabolic demands become correspondingly less. Thus it seems reasonable to conclude that a predegenerate graft—that is, one taken from the distal stump of a nerve—is more likely to survive the temporary avascularity of the initial period after transplantation. Seddon has pointed out that the use of predegenerated grafts has been recommended on other grounds; there seems good reason now to consider that they may be the material of choice when main-trunk grafts are used. It is true that

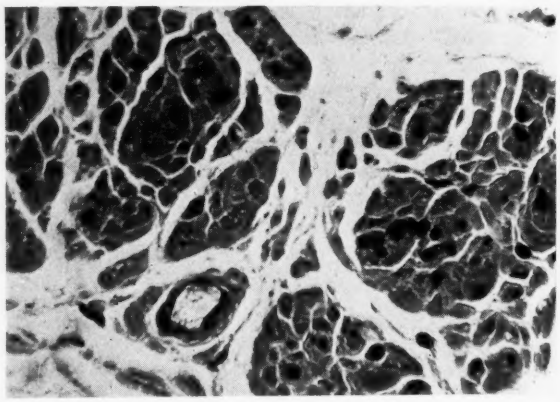

FIG. 172.—*Case R.*66. Detail of an area of excess collagenization. T. S. Masson. (× 560.)

long-standing degeneration may be harmful, but the graft will not be in any worse condition than the host distal stump, through which also the fibres must grow.

II. THE ENDONEURIUM OF THE DISTAL STUMP AND RECOVERY AFTER GRAFTING

Experimental studies of nerve-grafting have usually been carried out under conditions somewhat different from those present when a graft is used in man. The graft is placed in a gap created by the resection of a segment of nerve with the minimum of trauma and under aseptic conditions, and it is thus sutured to proximal and distal stumps that are in the best possible state for permitting regeneration. But in human cases the grafts are inserted at a secondary operation performed many weeks or months after an injury of exceptional severity—the operation being reserved for cases in which end-to-end suture is impossible. Hence the pathological changes are unusually extensive. In assessing the success of autografts we must, therefore, first determine whether the stumps to which they were sutured were in a satisfactory state: failure of recovery may be found to signify not a failure of the graft, but an inadequate resection of the stumps.

In all cases of nerve repair undertaken at the Oxford Centre the extreme proximal and distal surfaces of the resected segment are examined histologically: the sections so obtained represent the condition of the proximal and distal stumps at the suture line. On the basis of this investigation, correlated with the later observation of recovery, it has

been possible to form an opinion as to the degree of abnormality in the stumps that is compatible with good functional recovery. The full diameter of nervous tissue should be present in both stumps; it should be arranged in bundle form; and the connective tissue between the bundles should not be grossly increased by scarring. This theme has been discussed more fully elsewhere (Holmes, 1947), and the criteria derived from the study of end-to-end suture have been used to decide whether the stumps to which grafts have been sutured are in a satisfactory condition. Significant departures from a satisfactory state are recorded by Seddon (*Tables III–VII*, pp. 159–164). Here we are concerned with one particular feature of the suture line: that is, the state of the endoneurium in the distal stump. Abnormalities have been found most commonly in digital nerves, and we believe them to have been responsible for failure or a poor result after several grafting operations.

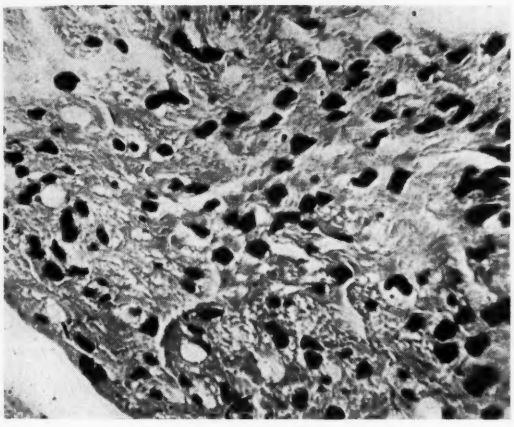

FIG. 173.—*Case S.*93. Distal stump. T. S. Masson. (× 560.)

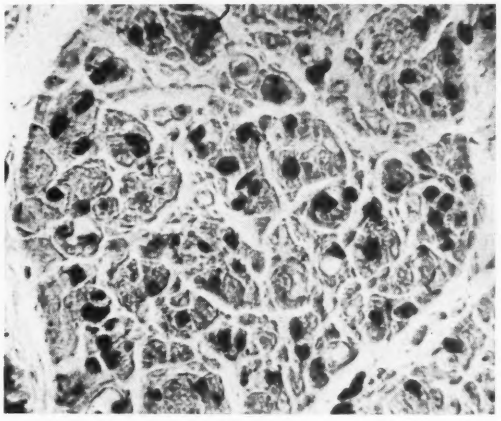

FIG. 174.—*Case S.*93. Distal stump. T. S. Masson. (× 560.)

It is now established that Wallerian degeneration is slowly progressive after division of a nerve, so long as the lesion is unrepaired. A normal nerve-bundle contains a connective-tissue framework, the endoneurium, and each nerve-fibre lies within a tube formed by the endoneurium. The larger tubes have a diameter of the order of 15μ; *Fig.* 168 gives an impression of the general architecture of normal nerve. Wallerian degeneration involves the destruction of the nerve-fibres; and all that remains of them within the tubes, now called Schwann tubes, is a row of Schwann cells which have long, thin nuclei and an elongated fibrous cytoplasm. The Schwann cells have a diameter far less than 15μ, and after about six weeks of Wallerian degeneration the lumina of the Schwann tubes containing them have shrunk to a diameter of the order of 2μ.

In consequence of the progressive nature of degeneration the 'normal' condition of the endoneurium of a distal stump is a function of the time that has elapsed between injury and exploration.

The most serious departure from the normal, which gravely hinders regeneration, is that of an undue collagenization of the endoneurium of the distal trunk. This not only tends to obliterate the Schwann tubes but also embeds them in a matrix of thick collagen fibres, which may hinder or completely prevent that redistension of the tubes that is an essential in the regeneration of normal-sized fibres.

Excessive endoneurial collagenization has regularly been found where peripheral nerves have suffered ischæmia in cases of Volkmann's contracture (Holmes, Highet, and Seddon, 1944). It has also been found in peripheral nerve when a traumatic division was complicated by vascular damage, even though the latter was too localized to produce muscular necrosis (Seddon and Holmes, 1945). However, it is relatively uncommon in the distal stumps of main nerve-trunks even when a neighbouring main blood-vessel has been divided. But it has been found with some frequency in cases of digital nerve injury, where there is of necessity concomitant damage of the digital vessels. It merits consideration as an important factor in determining the success of nerve-grafting in the hand.

The following selected cases demonstrate what may be regarded as normal and abnormal in the endoneurium of a distal stump. The photographic illustrations convey what is significant in the histology, and in order to facilitate comparison between the cases they are all reproduced at the same scale of magnification. Further reference to the cases chosen will be found in Seddon's paper (*Tables III–VII*, pp. 159–164). Each photograph is of a small area within a nerve-bundle at the distal suture line; the sections are cut transverse to the long axis of the nerve. Details of the histological technique are given elsewhere (Holmes, 1947).

*Case S.*93.—

Aug. 5, 1943: Digital nerve lesion.

June 14, 1944: Repair by autograft. There were four distal stumps: to the radial and ulnar sides of the thumb, to the radial side of the index, and to the third digit. *Figs.* 173, 174 are of the two stumps to the thumb respectively. Both are in a satisfactory condition, though they differ somewhat in appearances. The Schwann tubes are patent though small, and the endoneurial collagen is not dense or obliterating. The other stumps were similar.

Recovery good: *see Table III*, p. 159.

*Case C.*134.—

Oct. 12, 1944: Digital nerve lesion.

Jan. 17, 1945: Repair by autograft. Both distal stumps, to the index and 2nd cleft, were in a satisfactory

state. The latter is shown in *Fig.* 175. The Schwann tubes are wider than those in *Case S.*93, as is to be expected, since here degeneration had been proceeding

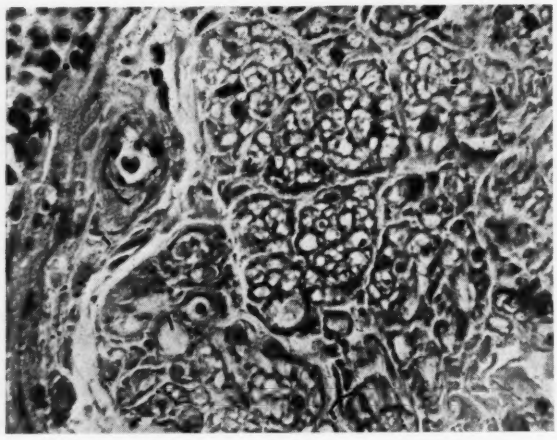

FIG. 175.—*Case C.*134. Distal stump. T. S. Masson. (× 560.)

for three months only. The tube lumina are extremely clear, and there is no excess of collagen.

Recovery good: *see* Seddon's paper, *Table III.*

*Case M.*96.—

April 17, 1944: Digital nerve lesion.

Nov. 4: Repair by autograft. All four distal stumps showed excessive collagenization of the endoneurium. *Fig.* 176 represents the condition of the stump

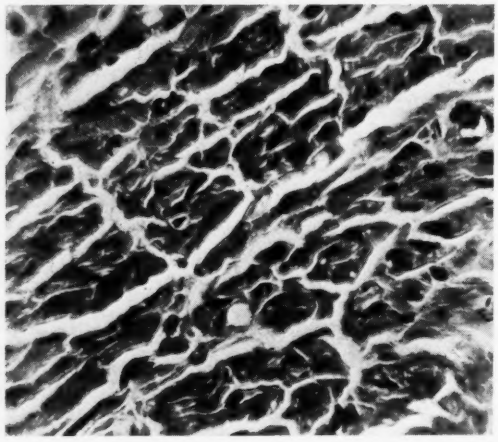

FIG. 176.—*Case M.*96. Distal stump; excess collagenization. T. S. Masson. (× 560.)

to the radial side of the index. The others were similar. Schwann tubes are visible, but they appear only as tiny cracks in a continuous network of dense collagen fibres. It seems most unlikely that such a solid mass could be distended to allow the regeneration of nerve-fibres within the tubes. The prognosis was considered to be unfavourable.

Recovery: none.

*Case P.*55*A.*—

May 22, 1943: Digital nerve lesion.

Feb. 16, 1944: Repair by autograft. The two distal stumps, to the index and second and third digits, both showed excessive endoneurial collagen (*Fig.* 177). *Fig.* 178 is a low-power view of part of the distal stump of the nerve to the second and third digits. It shows an accompanying artery with its lumen almost completely obliterated, and the dense endoneurial collagen in the bundles is somewhat shrunken and distorted. The condition of the nerves was similar to that in *Case M.*96, but *Fig.* 177, compared with *Fig.* 176, shows how a

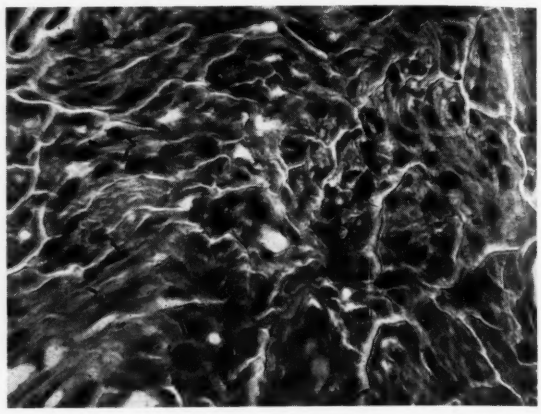

FIG. 177.—*Case P.*55*A.* Distal stump; excess collagenization. T. S. Masson. (× 560.)

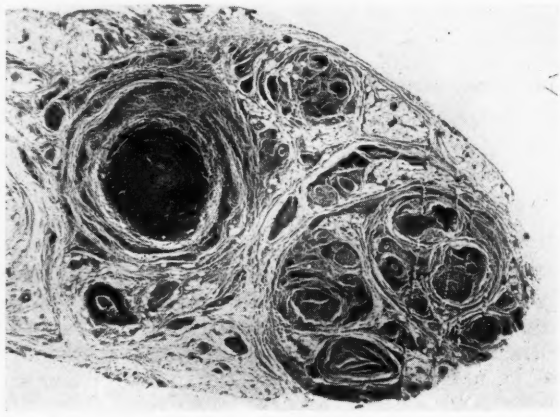

FIG. 178.—*Case P.*55*A.* Low-power view of part of the distal stump, showing an accompanying artery with obliterated lumen. T. S. Masson. (× 12.)

different appearance may be given when some of the tubes run obliquely to the plane of section. It was thought that a good recovery could not be expected.

Recovery: unfortunately the patient was killed in an accident on *Sept.* 29, 1944. There was no recovery when he was last examined on *Sept.* 26. The case is excluded from Seddon's tables.

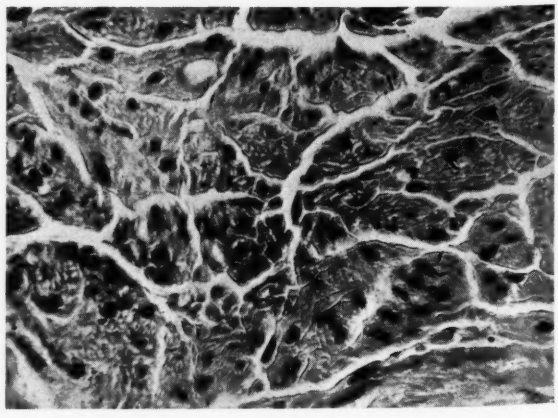

FIG. 179.—*Case R.*75. Distal stump; excess collagenization. T. S. Masson. (× 560.)

Case R.75.—
Aug. 25, 1944: Median nerve lesion.
Sept. 5, 1945: Repair by autograft. Here again the distal stump shows restricted Schwann tubes embedded in a solid collagenous matrix (*Fig.* 179). A good quality of recovery seemed unlikely.
Recovery: none.

DISCUSSION

Ischæmic collagenization of nerve, unlike Wallerian degeneration, is a regional process: it is localized to those stretches of the nerve that have suffered from an excessive degree of interference with their blood-supply. So it is possible that a more generous resection of the distal stump in our unsuccessful digital grafts would have exposed a suture line with a normal endoneurium. Thus, although we have no direct evidence in support of this suggestion, it is clear that the wisest course in digital nerve operations is to make the distal resection as extensive as is possible.

SUMMARY

Biopsies were taken from two grafts, each formed of two parallel lengths of the lateral popliteal nerve, and placed sixteen and twenty-two months previously in a gap in the medial popliteal nerve. In both cases the lateral popliteal had itself been divided by the original injury. Three of the grafted lengths of nerve were taken from the distal stump and so were predegenerated; these were found to be satisfactorily re-innervated. One of the grafted pieces was taken from the proximal stump and so was normal when transplanted; the biopsy from this nerve was necrotic and there was no evidence of regeneration.

In three cases nerves were experimentally transplanted and later examined histologically. One transplant was of a segment of the posterior interosseous nerve and was sutured to a normal proximal stump. It was found to be abundantly re-innervated and normal in all respects. Two segments of the radial nerve were treated as free transplants; they showed some abnormalities of degeneration but none so severe as to prevent their serving as successful grafts.

It is concluded that full-thickness autografts offer considerable prospects of success. Grafts taken from the distal stump of a divided nerve may be more successful than those from the proximal stump, since they are better able to survive the temporary ischæmia of transplantation.

Excessive collagenization of the endoneurium in the distal stumps of digital nerves is considered to be an important cause of failure in grafting operations in the hand. The degree of collagenization that is incompatible with recovery is illustrated and compared with the normal state. The condition is attributable to the ischæmia consequent on injury to the digital vessels. The resection of the distal stumps should be as generous as possible in digital nerve operations.

Similar changes are occasionally found in the distal stump after division of a main nerve-trunk, where the injury has been of great severity and has damaged adjoining blood-vessels.

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CLEFT PALATE AND THE MECHANISM OF SPEECH*

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THE main disability of the cleft-palate patient is the defect in speech. The operation for repair of the palate and nasopharyngeal valve is merely the first stage of treatment. It is incumbent on the surgeon who has undertaken the treatment of one of these patients to supervise the after-care until normal speech has been attained. To complete this final stage it is important for the surgeon to understand the mechanism of normal speech.

In the evolution of man, speech is one of the most recent intellectual acquisitions. The centre governing this faculty in the brain has not been accurately localized. At present the known sensory and motor projection centres occupy only a small part of the entire cortex. According to Ranson (1925), the remaining parts are connected with these by association fibres, and are known as 'association centres',

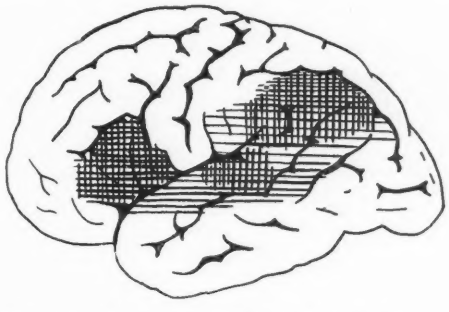


Fig. 180.—Speech centres of the left cerebral cortex.
1. *Afferent*:—
   a. Auditory: Posterior part of left superior temporal gyrus.
   b. Visual: Angular and supramarginal gyri.
   c. Kinæsthetic: Near the centre of the parietal cortex.
2. *Motor*: The triangular and opercular portions of the left inferior frontal gyrus.

*An Arris and Gale Lecture delivered at the Royal College of Surgeons of England on Feb. 12, 1940. The first part of this lecture describing the anatomy, aetiology, and operative treatment was published in this JOURNAL in 1941, **29**, No. 114, 197–227.

or ' centres of intellect '. For instance, the intermediate precentral area is especially concerned with the execution of complex and skilled movements in which conscious volition takes an active part. The increased size of the human cerebral hemisphere over that of all animals which cannot speak rationally, is due to the greater development of these ' association centres ' in man.

It is now generally believed that, in right-handed people, there is a widespread area on the left side of the brain concerned with speech. Marie (1917) includes in the speech area on the left side of the brain the whole of the temporosphenoidal lobe, much of the parietal lobe, the island of Reil, and the lower frontal convolutions. (*Fig.* 180.)

MECHANISM FOR THE PRODUCTION OF SPEECH SOUNDS

Speech is dependent on the activity of these special regions of the cerebral cortex and is effected by motor impulses to the muscles concerned in the production and modification of sound. Lightning action and perfect co-ordination of the muscles of the three components of the speech mechanism are essential :—

1. *Expiration* of air from the lungs :—
   Diaphragm, abdominal, and intercostal muscles.
2. *Phonation* or vibration of air :—
   Vocal cords vibrate by aerodynamic action. Tenseness and position by thyro-arytenoid muscles.
3. *Resonance and Articulation* :—
   a. Pharyngeal—a trumpet action.
   b. Buccal—articulation ; lips, tongue, teeth, nasopharyngeal valve.
   c. Nasal—used only in English speech for " M ", " N " and " NG " sounds.
   False vocal cords providing resonance and sometimes occlusion.

Air is expelled from the lungs by the upward excursion of the diaphragm, reinforced by the contraction of the abdominal and intercostal muscles, which draw the ribs downwards.

When voiced sounds are produced, the vocal cords are made to vibrate as air passes through the larynx, by aerodynamic—not muscular—action. The addition and modification of the voice are effected by the action of the thyro-arytenoid muscles, which alter the position and tension of the cords.

Sir Richard Paget (1930) and Professor Oscar Russell (1938) have emphasized the importance of the ventricular bands, or ' false vocal cords ', in speech production. Professor Oscar Russell has designed an ingenious laryngeal periscope (*Laryngo-periskop*) and has shown, by high-speed motion pictures of his own ventricular bands during speech, that complete occlusion may occur between these ; and he believes that this is the natural mechanism in rapid speech for consonant combinations such as ' it/comes'.

The most rapid and intricate muscular movements carried out during articulation would appear, however, to occur in the mouth and pharynx. The pharynx acts as a resonator, like a trumpet or loud-speaker horn, and if its action is excluded—as in certain cases of cut throat—the voice is monotonous and without resonance ; the consonant sounds are indefinite and resemble those in cleft-palate speech.

The niceties of sound modification and articulation are effected by the action of the muscles of the lips, tongue, soft palate, and the nasopharyngeal sphincter.

There are four kinds of speech sounds : (1) Vowels ; (2) Diphthongs, or compound vowel sounds (e.g., ' iu ' as in ' few ') ; (3) Consonants ; (4) Affricates, or compound consonant sounds (e.g., ' ch ' as in ' chair ' = Tsh).

Vowels.—These are produced by the voice and there is no obstruction to the escape of air. The lips are kept open, but the nasal cavities are partially excluded by the soft palate. Most vowel sounds are easily pronounced by cleft-palate patients, but they are sometimes formed with a nasal intonation if the nasopharyngeal sphincter is incompetent. The most difficult vowel sounds for these patients are ' oo ' and ' ee '.

Consonants.—In the production of consonant sounds, on the other hand, there is always some *obstruction* to the escape of air. The character of the sound produced depends upon : (*a*) The site of obstruction ; (*b*) The degree of obstruction ; (*c*) The position of the soft palate ; (*d*) The presence or absence of the voice.

a. The Site of Obstruction.—When teaching a cleft-palate patient to pronounce the consonant sounds with which he has most difficulty, it is a great help to be able to show him exactly where to place his lips and tongue (*see* p. 176). Charts showing the various positions have been used by speech trainers for a long time. Some of these are most instructive ; some misleading. In the case of certain sounds produced with the mouth partially closed, the exact position of the tongue and palate has often been a matter of conjecture based upon the personal impression of the elocutionist. Scientific experiments have been undertaken by Barclay and Nelson (1922) and Stephen Jones (1929) by means of radiography, which have shown certain fallacies in the previously accepted positions.

We carried out some experiments in an attempt to elucidate the position of the tongue, lips, and palate during the production of speech sounds. Some bismuth meal was taken to coat the lips, tongue, and palate ; lipiodol was injected along the floor of the nose and on the upper and lower surfaces of the soft palate. Radiographs (*Figs.* 181-184) were taken by Dr. A. S. Johnstone during the articulation of various sounds.

In severe cases of cleft palate in which there is no possibility of producing oral interruption to the escape of air, so essential for the formation of consonant sounds, the true, or possibly the false, vocal cords close abruptly to secure interruption of the efferent air-stream. When the glottis is suddenly released the pent-up air escapes with a rush, and when the tongue and lips are placed correctly, a fair imitation of many consonant sounds is produced. More often, however, this ' glottic stop ', as it is called, replaces the proper oral occlusion used in the formation of true consonant sounds and serves merely to separate the vowel sounds in a word (e.g., ' Peter '

becomes ' e/er '). Such speech is usually difficult for strangers to understand.

In other cleft-palate patients, occlusive, rabbit-like movements of the nostrils are made during speech in an attempt to limit the escape of air. Many suffer from shortness of breath while speaking

Fig. 181.

Fig. 182.

Fig. 183.

Figs. 181-183.—Radiographs taken by Dr. A. S. Johnstone during the production of consonant sounds. *Fig.* 181, 'P' —The lips are closed; the tongue is flattened. *Fig.* 182, 'Th'—The tip of the tongue is between the incisor teeth. *Fig.* 183, 'K'—The tongue is arched upwards to touch the anterior segment of the soft palate. The middle third of the soft palate is raised in all these oral consonant sounds to occlude the nasopharyngeal isthmus.

due to loss of air through the nose. This is a serious handicap, because, for some reason, they tend to speak more rapidly than other folk. Possibly they believe that the slurring of words in rapid speech may hide their disability; in reality their speech is made less intelligible and they should all be trained to talk more slowly than normal people.

b. The Degree of Obstruction.—

i. *Plosives*: In the formation of plosives there is a momentary complete obstruction, followed by a sudden escape of air. They are produced by an explosion of air bursting through some barrier (such as the lips, when 'P' and 'B' sounds are formed). They have no duration and the sound stops immediately.

ii. *Fricatives* are produced by friction when the obstruction is incomplete and air whistles through a narrow opening. The sound lasts as long as the breath lasts, and is associated with vibration of the lips or tongue. 'V' and 'R' are examples.

c. The Position of the Soft Palate.—

i. *Oral consonants*: Air should escape only through the mouth in all consonant sounds, except 'M', 'N', and 'NG'. With these exceptions, if pure clear sounds are to be formed, it is essential for the nasal cavities to be shut off from the mouth by the palate and the nasopharyngeal sphincter (*Fig.* 184 A).

ii. *Nasal consonants*: For the correct pronunciation of 'M', 'N', and 'NG' sounds, air is directed outwards through the nose. The mouth is closed and the nasopharyngeal valve is open (*Fig.* 184, B).

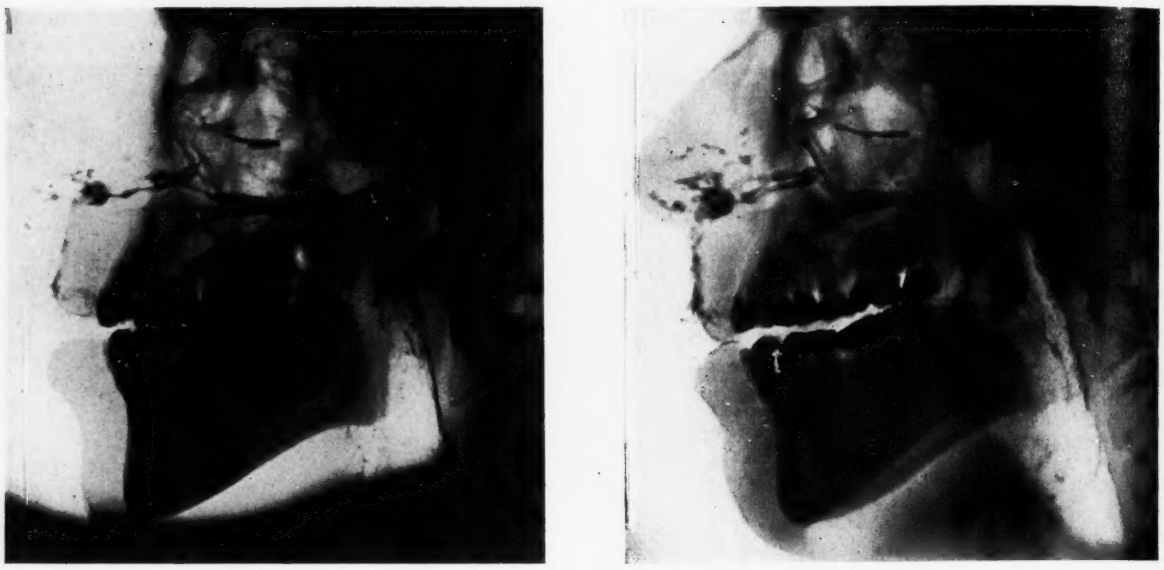
d. The Presence or Absence of the Voice modifies the type of consonant sound produced, for instance, the 'F' sound is made by the breath only, while the 'V' sound is formed in a similar way, except that the voice is used and the cords vibrate.

Consonant sounds which cause the greatest difficulty for cleft-palate patients are those which are formed by the most forcible compression and explosion of air through the mouth. For these sounds any leakage of air into the nose is disastrous. Consonant sounds which may be difficult for cleft-palate patients may be tabulated in order of severity :—

S
K G
T D
Th
P B
L F V

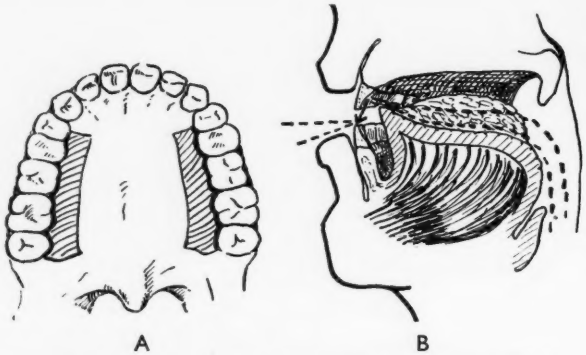
The 'S' sound, being the most troublesome for cleft-palate patients, assumes especial importance. It is produced under normal conditions by a stream of air which passes along a groove down the centre of the tongue. When the stream meets the posterior surface of the upper incisor teeth it is diverted downwards and, as the air sweeps upon the cutting edges of the lower incisor teeth, a hissing or whistling sibilant sound is produced. To guide this stream of air, the sides of the tongue are raised to touch the sides of the hard palate and the tongue is grooved on its dorsal surface. The tip of the tongue is placed just behind the gap between the cutting edges of the incisor teeth. The lips are parted as if beginning to smile. (*Fig.* 185).

Competence of the nasopharyngeal valve is necessary to provide an adequate stream of air through the mouth ; accurate tongue control is also required.



A B

Fig. 184.—Radiographs by Dr. A. S. Johnstone, taken during the production of : A, An oral consonant sound ; the nasopharyngeal valve is closed. B, A nasal consonant sound ; the nasopharyngeal valve is open.



A B

Fig. 185.—'S' sound. A, Diagram showing the area of the palate which comes into contact with the sides of the tongue ; B, Sagittal section, showing the grooving of the tongue and the direction of the air-stream.

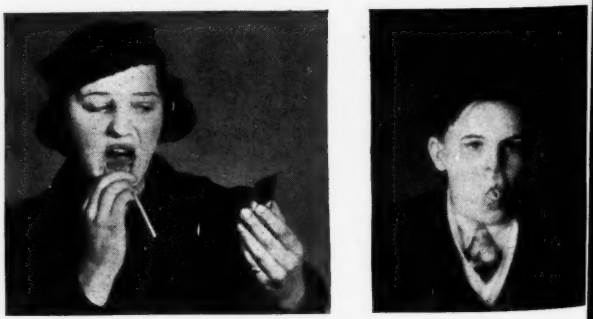


Fig. 186.—Photographs showing cleft-palate patients learning to groove their tongues to form the correct 'S' sound.

Many cleft-palate patients make a husky sound, to replace the correct sibilant 'S', by whistling a stream of air between the back of the tongue and the pharyngeal wall. This sound can be produced with the mouth wide open, which is impossible with the normal 'S'.

A useful method of training a patient to make the correct sound is to block the nostrils with wool, and then, by placing a straw down the centre of the grooved tongue, the relationship of the tongue to the

teeth is demonstrated; the patient whistles the 'S' sound down the straw. Later the straw is removed and finally the wool. (*Fig.* 186.)

After repair of the nasopharyngeal sphincter and the palate, other factors may prejudice intelligible speech:—

1. *Psychological causes*: Shyness; ridicule at school, leading to an inferiority complex.
2. *Irregularity of the upper incisor teeth.*
3. *Stiffness of the upper lip*, if there has been a hare-lip.
4. *Deafness*, owing to frequency of otitis media in cleft palate cases.

Orthodontic treatment by a dental surgeon will in most cases readjust the alinement of displaced teeth. Many patients who have especial difficulty with sibilant sounds improve considerably after adjustment of their incisors.

Tightness and stiffness of the upper lip is treated by massage, lip exercises, and, in the severe cases, by epithelial inlay.

Any operative treatment which is not followed by systematic speech training is, in our experience,

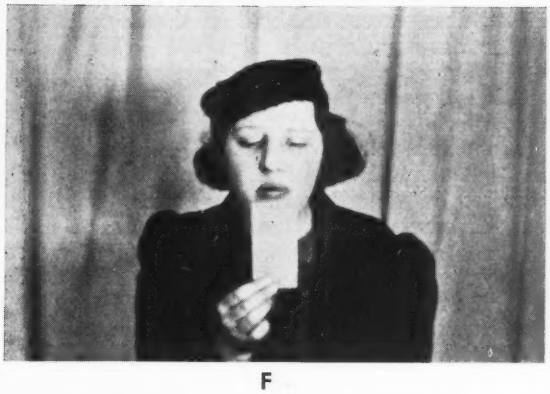
A

D

B

E

C



F

Fig. 187.—Photographs of speech training class.

sadly incomplete. Regular classes under the guidance of a fully-qualified and enthusiastic speech trainer are of inestimable value in the education of breath control and the use of the lips, tongue, and nasopharyngeal sphincter. But these classes are helpful in many other ways.

Schoolchildren can be cruel in harsh criticism and ridicule of abnormality in another. When a child with a cleft palate is old enough to become self-conscious he may lose his self-respect and shun his fellows. A vicious circle is set up which originates in ridicule, leads to shyness, and progresses to aversion and fear of others and their conversation. The inferiority complex is soon firmly established.

When cleft-palate children come to a class with others who have difficulties similar to themselves, they gradually lose their shyness, although this may take some weeks. The time varies with the patience, optimism, and enthusiasm of the speech trainer and the intelligence of the child's mother. Speech classes (*Fig.* 187) serve to recruit the interest of the mothers in their children's speech welfare. If the mothers are invited to watch the classes, they soon become interested, and most will practise the difficult sounds with their children at home.

Ideally, each child should have training once or twice a week in a class, as well as individual coaching for short periods each day at his home. Boredom is the *bête noire* of every child, and for this reason all classes must be short and made amusing by a variety of games. For the older patients, pictures showing the position of the tongue and lips in the pronunciation of important sounds, are hung upon the wall, so that they can easily be seen by the patients and used for demonstration by the speech trainer. A large mirror hung upon the wall, or a small one held in the hand (*see Fig.* 186), is often useful to patients in their efforts to control the tongue and lips.

It is wise to divide the patients into three classes: (1) Infants under 3 years; (2) Children—3 to 12 years; (3) Adolescents and adults.

No class should last more than one hour and during this time hard work is camouflaged with games, rhymes, and songs. Infants and the younger children learn to use their soft palates and nasopharyngeal spincters by blowing soap bubbles, toy balloons, and a variety of whistles. Many of the older patients must be trained to discard their bad habits of speech, like the 'glottic stop', before learning the correct methods of pronunciation.

The programme is in general:—

1. *Blowing games and breathing exercises* to teach nasopharyngeal occlusion.
2. *Vowel practice.*
3. *Consonant practice* with a mirror (being the essential element of the whole programme, this is described in some detail below.)
4. *Sentences.* Each patient is taught to say the words slowly in a loud voice and without effort or grimace.
5. *Rhymes and songs.*
6. *Reading aloud* in class and at home.

Speech training helps to develop the intellect as well as the speech mechanism, and, more important still, it brings happiness and confidence and dispels misery and fear. The patience of the speech-trainer, the keenness of the mother, and the enthusiasm of the patient are the keynotes of success.

CONSONANT PRACTICE

Table of Consonants

Site of Obstruction to the Escape of Air	Oral				Nasal
	Plosives		*Fricatives*		
	Breath	Voice	Breath	Voice	
Lips	P	B		W	M
Lower lips and upper teeth			F	V	
Tip of tongue between teeth			Th	Th	
Tip of tongue behind upper teeth	T	D		L	N
Tip of tongue behind lower front teeth; sides of tongue raised to touch inner side of upper teeth			S SH	Z ZH	
Tip of tongue vibrating against front of palate, sides of tongue raised			R	R	
Back of tongue arched against palate	K	G		Y (Yes)	NG
Mouth open, tongue flat			H		

PLOSIVES

'P'—The lips are pressed together, and the breath is then allowed to burst through suddenly, making a small explosion.

'B'—As 'P', but the voice is used. The lips are pressed together, and the voice bursts through.

'T'—The tongue is pressed behind the upper incisors, then the tongue is blown away, using the breath only.

'D'—As 'T', but the voice is used.

'K'—The back of the tongue is raised to touch the palate. The tip of the tongue is behind the lower incisors. Only the breath is used.

'G'—As for 'K', but the voice is used.

FRICATIVES

'F'—The lower lip is placed under the upper incisors. The breath is blown through the slit.

'V'—As for 'F', but the voice is used.

'TH'—The tip of the tongue is placed between the incisor teeth, and breath is blown through the slit.

'S'—The tip of the tongue is placed just behind the gap between the cutting edges of the incisor teeth. The sides of the tongue are raised to touch the sides of the hard palate. A groove is thus made down the centre of the tongue and along this groove a stream of air is driven through a narrow gap between the cutting edges of the incisor teeth. A hissing or whistling sound is thus produced.

'Z'—As 'S', but the voice is used.

'SH'—As 'S', but the groove in the tongue is wider. The tip of the tongue is drawn back a little more than in 'S', and the sides are not quite so high.

'ZH' (Pronounced as in 'measure')—As 'SH', but the voice is used.

'W'—The lips are rounded and the voice comes through continuously.

'Y' (pronounced as in 'Yes')—The lips are spread. The tongue is arched. The voice comes through the slit continuously.

'L'—The tip of the tongue is placed behind the upper incisor teeth. The part of the tongue just behind the tip touches the inner side of the gums of the teeth behind the incisors. The sides of the tongue drop down, and air escapes over the sides. (The tongue position is opposite to that in 'S'.)

'R'—The tip of the tongue vibrates against the front of the hard palate, and the sides of the tongue are raised.

'H'—The tongue is kept flat, causing no obstruction in the mouth. Air is blown out with the mouth open.

SUMMARY

The physiology of the normal speech mechanism is described briefly. A radiographic method of demonstrating the position of the soft palate, lips, and tongue during the articulation of speech sounds is described. Cleft-palate speech defects are discussed, and the methods of speech training after repair of the palate and nasopharyngeal sphincter are described.

I should like to express thanks to Dr. A. S. Johnstone for taking all the radiographs himself, and for his kind help and advice. I should also like to thank Miss Hewitt, Miss Knowles, Miss Brierley, Mrs. Andrews, and Mrs. Jackson for their enthusiasm in the training of my cleft-palate patients.

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PHÆOCHROMOCYTOMA

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FROM THE DEPARTMENT OF PATHOLOGY AND THE WARDS OF THE ROYAL INFIRMARY, GLASGOW

PRIMARY tumours of the suprarenal, apart from those occurring in early life (Blacklock, 1934), are a rarity. Over an eight-year period, 1937–44, 13 primary growths were found in the suprarenals of 2994 cases examined *post mortem* at the Glasgow Royal Infirmary. Of these, 11 were adenomatous tumours of the cortex and 2 tumours of the medulla, one being a neuroblastoma and the other a phæochromocytoma. During the same interval, 55 secondary growths were observed in the suprarenals. Most primary tumours of the suprarenal medulla have a developmental origin, being derived either from the undifferentiated sympathogonia or the more differentiated sympathicoblasts. In the majority of cases these primitive cells form neurogenic tumours such as sympathicoblastoma (neuroblastoma) and ganglioneuroma: more rarely they give rise to chromaffin tumours to which the names 'chromaffinoma', 'phæochromocytoma', and 'paraganglioma' have been applied. The terms 'phæochromocytoma' and 'chromaffinoma' are usually reserved for tumours arising in the adrenal medulla, 'paraganglioma' being applied to growths arising elsewhere in the sympathetic nervous system. Phæochromocytomata are of rare occurrence, McKeith (1944) being able to collect only 152 cases from the literature. Most of the reported cases have been autopsy findings, but since the review of Rabin (1929) the diagnosis has been made during life with increasing frequency. The clinical diagnosis is usually made on the basis of attacks of paroxysmal hypertension, the first clear description of which was given by Labbé, Tinel, and Doumer in 1922. Reviews of the literature have been published by Rabin (1929), Eisenberg and Wallerstein (1932) (*Table I*), Belt and Powell (1934), Howard and Barker (1937), McKeith (1944), and others (*Tables II, III*). Chromaffin-celled tumours are, however, not peculiar to the suprarenal medulla as they (paragangliomata) have been reported in other parts of the chromaffin system such as the carotid body (Goodof and Lischer, 1943) and the organ of Zuckerkandl (Podloucky, 1940).

The tumours give rise to a symptom-complex which would appear to depend on the discharge of adrenaline or an adrenaline-like substance into the blood-stream. The demonstration of an adrenaline-like pressor substance in the blood during attacks by Beer, King, and Prinzmetal (1937) has since been confirmed (Strombeck and Hedberg, 1939). Assay of the tumour for adrenaline by many authors has revealed a very high content.

In the present paper 6 cases of phæochromocytoma, 5 of which came under our observation in a very short period, are described. Previous to their occurrence only 1 case had been found in the above series of 2994 post-mortem examinations carried out in this hospital over an eight-year period, though in all autopsies both suprarenals were examined. The clinical recognition of these tumours is of some importance owing to the success of surgical removal of the growth as described by Biskind, Meyer, and Beadner (1941) and Hyman and Mencher (1943).

* With the co-operation of Professor Archibald Harrington, A. Kennie, A. Muir Crawford, and J. Ralston.

HISTOLOGICAL METHODS

The histological investigation of chromaffin tumours demands special methods. In our cases portions of the tumours were fixed for a few hours in 10 per cent neutral formol and thereafter transferred to one of the following fixatives, viz., Zenker (without acetic acid), Müller, Bouin, and formol corrosive. Small portions were also fixed directly in absolute alcohol. It was observed that portions left in the formol solution and exposed to diffuse daylight became fairly quickly light brownish in colour, while those transferred to Zenker and Müller developed a much deeper brown tint, that in the Müller being almost black. This brownish colour did not fade on exposure to air or light or when portions of the growth were preserved in glycerin, which became brownish. Sections were prepared by the paraffin process and also by freezing. Paraffin sections were stained by hæmatoxylin and eosin,

Table I.—CASES REPORTED FROM THE LITERATURE BY EISENBERG AND WALLERSTEIN (1932)

BLOOD-PRESSURE	AGE GROUPS								NO. IN SERIES
	Not Stated	1–10	10–20	20–30	30–40	40–50	50–60	60+	
Paroxysmal			Fränkel	Labbé, Azerad, and Violle; Labbé, Tinel, and Doumer; Mayo; Oberlung and Jung; Shipley	Vaquez et al.; Biebl and Wichels; Zeckwer	Barker; Connor (3); Orth; Neusel and Wiesel		Lascagna	16
Persistent						Rabin			1
Hypertension only mentioned	Kerpola					Bergstrand; Herde (2); Robert; Schroeder; Helly		Thomas	7
No mention	Masson (2); Neusel and Wiesel (1); Bonnamour et al.	Wahl (2½ y.)	Marchetti		Hedinger; Wagelin; Weber; Laignel-Lavastin and Aubertin	Harbitz; Masson and Martin	Herxheimer	Berdez; Herde (1); Perley; Suzuki (1, 2, 3); Manasse (1, 2)	21
Normal				King	Kawashima	Riemer; Gravier and Bernheim	Lazarus and Eisenberg; Rossum and Barry; Eisenberg and Wallerstein		7

Note.—Figure in brackets after name denotes the number of the case in the paper quoted.

Table II.—CASES REPORTED FROM THE LITERATURE BY EDWARD (1937).

BLOOD-PRESSURE	AGE GROUPS								NO. IN SERIES
	Not Stated	1–10	10–20	20–30	30–40	40–50	50–60	60+	
Paroxysmal			Collier et al.; Ernould and Picard; Paul (1)	Suermondt; Von Der Mühll; Paul (3)	Bauer and Leriche; Kelly et al.; Nordman and Kalk; Porter and Porter; Appelmans and Van Goidsenhoven; Volhard; De Wesselow	Belt and Powell; Kahlau; Rogers; Sachs and Russum; Sevki; Tillman	McKenna and Hines	Paul (2)	21
Persistent			Kremer	Edward				Hick	3
Hypertension only mentioned					Paul (4)	Görog; Kaulback; Popken	Paul (5)		5
No mention						Buchner			1
Normal	Fingerland; Popken; Bianchedi			Fein and Carman					4

Note.—Figure in brackets after name denotes the number of the case in the paper quoted.

Table III.—CASES REPORTED IN THE LITERATURE SINCE 1937, INCLUDING AUTHORS' OWN SERIES

BLOOD-PRESSURE	AGE GROUPS								NO. IN SERIES
	Not Stated	1–10	10–20	20–30	30–40	40–50	50–60	60+	
Paroxysmal		Neff et al.	McCullagh and Engel (1); Hyman and Mencher (4); Holst (1); Holst (2); Evans and Stewart	Van Epp et al. (1); Hyman and Mncher (1); Hyman and Mencher (2); Broster and McKeith; Boman and Wells; McKenzie and McEachern; Tenenbaum; Burgess et al.; Binger and Craig; Holst (3); McCullagh and Engel (2); Kirshbaum and Balkin (1); Palmer and Castleman; Blacklock and Symington (1)	Nettleship; Biskind et al.; Van Epp et al. (2); Hyman and Mencher (3); Kenyon; Landau; Strombeck and Hedberg; Rodin; Baker and Reinhoff; Blacklock and Symington (2)	Brunschwig and Humphreys Heath and Cahill; Borch-Johnson; Borras and Mota; Eleosser; Allen; Pincoff	Nuzum and Dalton	Howard and Barker	39
Persistent				Kirshbaum and Balkin (2); Oppenheimer and Fishberg	Thorn et al.; Blacklock and Symington (3)				4
No mention		Wahl and Robinson							1
Normal					Blacklock and Symington (6)	McGavack et al.	Blacklock and Symington (4); Rosenthal and Willis	Blacklock and Symington (5)	5

Note.—Figure in brackets after name denotes the number of case in the paper quoted.

Mallory, Masson's trichrome, and for reticulin. Frozen sections were stained by Sudan III for fat and celloidin sections by Best's carmine for glycogen. Paraffin sections were also stained by special methods to demonstrate chromaffin granules. The earliest method for this purpose is usually ascribed to Henle (1865), who showed that the cells of the chromaffin tissue turned brown after treatment with solutions of potassium bichromate due to a brown precipitate forming in the cells. This reaction is known as the chromaffin reaction. Later Ogata and Ogata (1917) showed that the brown precipitate was probably chromium dioxide. This reaction takes place most readily in a neutral medium, the presence of acid or alkali interfering with the reaction, as for example in solutions of Zenker containing acetic acid. Sections were stained by Schmorl's Giemsa method (1928) to demonstrate the adrenaline-like granules, but we failed to obtain good nuclear differentiation by the original method or by Sevki's modification (1934). By placing the sections after fixation in bichromate in a 0·2 per cent solution of potassium permanganate and rinsing in a 1 per cent solution of oxalic acid and thereafter proceeding as described by Sevki, much better results were obtained, the nuclei staining bluish and the granules an olive-green colour.

In any tumour such as the phæochromocytoma, which has a hormonal effect, an attempt should be made to carry out biological tests for the presence of active hormone in the growth. Unfortunately owing to war conditions or post-mortem changes, this was possible in only one of our cases.

CASE REPORTS

Case 1.—

CLINICAL FINDINGS.—The patient, a soldier, aged 21, was admitted to hospital from abroad on Oct. 6, 1943. He had enjoyed good health until ten months previously, when he was awakened from his sleep in the early morning with severe headache, palpitation, and breathlessness. These symptoms passed off in about five minutes. Thereafter he remained well for about six weeks, when a similar attack occurred. Following this, attacks became progressively more frequent, until he was having as many as five in the day. The attacks lasted one to two minutes only, after which he experienced a feeling of warmth throughout the body. Observation in a hospital abroad had revealed the association of his attacks with paroxysms of hypertension and suggested the possible presence of an adrenal medullary tumour. He was repatriated for further investigation. On his journey home and while in this country prior to admission to hospital—a period of three weeks in all—he suffered only occasional short attacks of palpitation. There were no relevant features in the past or family history.

Inspection showed a slightly-built man of average height and good musculature. The blood-pressure between attacks was variable, but tended to be slightly raised, between 130/80 and 160/85. Physical examination was essentially negative, except that the lower pole of the right kidney could occasionally be palpated. There was no detectable cardiac enlargement and no

palpable thickening of the peripheral arteries. Examination of the fundi revealed no abnormality.

Description of the Attacks.—At first these occurred in the early hours of the morning, but later they took place at any time. Active exercise sometimes precipitated an attack; no other precipitating causes were noted. The attacks were characterized by the sudden onset of palpitation, and of a feeling of tightness in the chest with difficulty in breathing, followed by a pounding headache. Marked facial pallor and constriction of the larger peripheral vessels were observed. Two such attacks were witnessed in hospital. At the height of the attack the blood-pressure was 260/120; after five minutes it fell to 190/110 and three minutes later the reading was 175/90. Still five minutes later the blood-pressure was 150/85 and in a further five minutes 140/80. Subjective symptoms lasted only three minutes in the first attack witnessed, and one minute in the second. Immediately after these short periods the patient felt well.

LABORATORY INVESTIGATIONS.—Urine, clear, chemically and microscopically. Blood: R.B.C., 4·5 million/c.mm.; Hb. 85 per cent; W.B.C. 8400/c.mm.; Differential count—neutrophils 55 per cent, eosinophils 3 per cent, lymphocytes 36 per cent, monocytes, 6 per cent. Blood-sedimentation-rate within normal limits. Blood Kahn test, negative. Blood-urea, 30 mg. per cent. Urea-clearance test, 60 per cent normal. Blood-cholesterol, 200 mg. per cent. Serum-sodium, 327 mg. per cent. Serum-potassium, 18·8 mg. per cent. Glucose-tolerance curve, 70, 147, 92, 70, 70 mg. per cent. Excretion of 17-ketosteroids: Oct. 17, 10·65 mg. in 24 hours, and Nov. 30, 11·8 mg. in 24 hours. All these results are related to the periods between attacks when the patient was free from symptoms.

Radiography of the chest, pituitary fossa, straight X-ray of the abdomen, and intravenous pyelography revealed no abnormality.

PROGRESS.—The relatively severe attacks disappeared soon after his admission, so that only two such attacks were witnessed. He was, however, subject to frequent attacks of headache and dizziness lasting only a few seconds. He was never observed while in these, since they nearly always occurred while out walking. Attempts artificially to induce an attack by means of vigorous exercises were made on several occasions without result. Massage of the upper abdomen was ineffective, although on one occasion a symptomless rise of blood-pressure to 180/100 was recorded. He was kept under observation for some time, but minor bouts continued to occur. Retrograde pyelography was now performed and revealed descent of the right kidney.

OPERATION (April 26, 1944).—Great difficulty was experienced in anæsthetizing the patient, who had had a moderate amount of premedication, and trouble continued throughout the operation. No blood-pressure estimations were made during the operation. The incision employed was a lumbar extraperitoneal one on the right side, which was, however, extended up and over the eleventh rib. Every small vessel divided bled copiously and about forty separate ligatures had to be tied during the cutting of the muscles. The patient's breathing, which had been vigorous up to this stage, suddenly stopped and he became pale and blue about the lips. This took place even before the muscles had been divided completely and thereafter his condition was most unsatisfactory. The kidney was readily palpated and was found lying so high that even dislocation of the last rib upwards did not give a satisfactory exposure. On pulling the kidney down, however, a tumour of the adrenal was found lying in the depths of the wound above and medial to the kidney. This tumour was well encapsulated but had a number of large veins coursing over it. To improve the access and before handling the tumour the last rib was now resected, thus affording a much better exposure. A small tear in the pleura was made at this stage but was sutured. The tumour was partly freed and ligatures were applied to vessels coming to it from the region of the renal vessels and from the diaphragm. No further vessels were encountered and the tumour was removed. The cavity was lightly packed and the wound closed.

Though intravenous plasma had been given during most of the operation, when the patient left the theatre he was in very poor condition, being pale and collapsed, with shallow respirations.

POST-OPERATIVE PROGRESS.—For two hours following the operation the systolic blood-pressure was below the level of 50 mm. Hg in spite of repeated intravenous injections of adrenaline totalling 45 min. of 1–1000 adrenaline hydrochlor. (2·7 mg.) and 10 c.c. eucortone. Thereafter rapid but transient rises to 120 mm. Hg and over followed subsequent doses of adrenaline intravenously. Between these doses the systolic pressure fell again to levels of about 50 mm. Hg. Accordingly a continuous intravenous adrenaline drip in saline was employed, the amount of adrenaline administered varying between 0·0346 and 0·0686 mg. per minute. With this procedure the blood-pressure was maintained between levels of 80 and 90 mm. Hg. Whenever the drip was discontinued a dramatic fall in the blood-pressure readings occurred. In spite of this therapy, blood and plasma transfusions (2 pints of each), and a further three injections of 10 c.c. eucortone, the patient's condition steadily deteriorated. Only 3 oz. of urine were obtained by catheterization, representing the total volume excreted in 48 hours; the blood-urea then was 170 mg. per cent. Eight hours later the blood-urea had risen to 220 mg. per cent and estimation of the serum-sodium and serum-potassium gave figures of 276 and 21·4 mg. per cent respectively. At the end of the second day the amount of adrenaline given by intravenous drip was doubled. The blood-pressure rose to systolic levels of 140 mm. Hg, but in the six hours preceding death, which took place 62 hours after operation, it showed a gradual decline, and registered a level of 80 mm. Hg immediately prior to death.

POST-MORTEM FINDINGS.—The body was that of a well-built young man. The face was congested and cyanosed and there was a slight yellowish coloration of the skin suggestive of early jaundice. A surgical wound in which packing was inserted was present in the right loin.

The pericardial sac was healthy. The heart (400 g.) was enlarged, due to a concentric hypertrophy of the left ventricle. The myocardium showed no fibrosis, the coronary arteries were healthy, and the valves all appeared normal. No lesion was present in the left lung. That on the right side showed many adhesions over the apex; the lower and middle lobes were collapsed. The lower and posterior parts of the mediastinum showed slight interstitial emphysema.

The peritoneum showed no lesion. The stomach and bowels were much distended. The liver was very yellowish and felt distinctly greasy. Both kidneys were congested, but no gross morbid changes were present apart from some bruising around the upper pole of the right organ. Above the right kidney there was a space with ragged walls and filled with packing from which the suprarenal tumour had been removed. Above this the diaphragm had been cut, but the wound was secured with sutures. The urinary bladder was healthy. The left suprarenal appeared normal to the naked eye. The spleen was congested.

No lesion was observed in the brain, pituitary, or thyroid.

HISTOLOGICAL FINDINGS.—The tumour, received four hours after excision, measured 8 cm. by 6 cm. and weighed 86 g. (*Fig.* 188). It was well encapsulated, many prominent vessels being observed in the capsular tissue. The cut surface had a pinkish-white appearance, numerous small vessels being visible in the substance

of the growth, which was rather soft in consistence. No evidence of necrosis was noted. The tumour, after a few hours in formalin solution, became brownish in colour.

Microscopically the tumour was very cellular, being composed of large rather long polyhedral cells varying in their greatest diameter from 10 to 50 microns. The

FIG. 188.—*Case* 1. Right suprarenal with encapsulated tumour; portions of cortex attached above and below. (× $\frac{2}{3}$.)

growth was well encapsulated by a dense layer of fibrous tissue, outside of which the remains of the suprarenal cortex was observed. The tumour cells just under the capsule were smaller and rounder than those more centrally placed. For the most part the cells were closely packed together, though at places there were large spaces (the sinusoidal spaces) filled with eosinophil granular material and a few red blood-cells. In the hæmatoxylin and eosin preparations the cell cytoplasm, which was fairly abundant, was slightly acidophil and in some cells there were small accumulations of bluish granules. The cytoplasm of many of the cells showed numerous vacuoles. The nuclei, with one to three nucleoli, varied both in

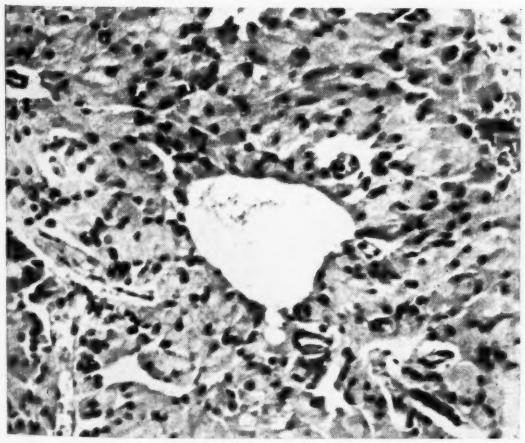


FIG. 189.—*Case* 1. Sinusoidal space surrounded by closely packed tumour cells. H. and E. (× 150.)

size and in shape, usually being eccentric in position. A very few cells showed mitosis. The cells were usually arranged in irregular alveoli which were separated from one another by strands of fine fibrous tissue. Towards the centre of many of these alveoli were large thin-walled sinusoidal spaces, the tumour cells lying immediately adjacent to the blood-cells (*Fig.* 189). The tumour was very vascular, many large capillaries being present in each low-power field. Around the capillaries the cells were rather closely packed: farther out the alveolar arrangement was more apparent.

In the tissue fixed in Müller's solution for some weeks, fine brownish granules were noted in sections scattered throughout the cytoplasm of some of the cells due to the reduction of the bichromate. In sections fixed by this

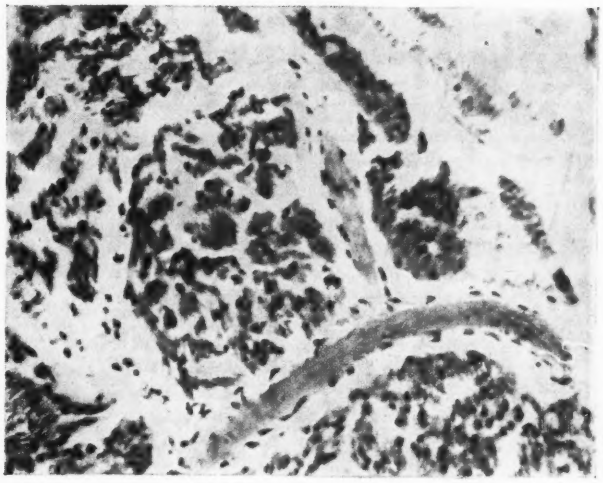


FIG. 190.—*Case* 1. Stained by Sevki's modification of Schmorl's Giemsa method to show adrenaline reaction (greenish) in tumour cells and also in serum in venules. (× 150.)

method and stained by the modification of Sevki's method quoted above, fine granules which had an olive-green colour were observed in the cytoplasm of a few of the cells. These greenish granules corresponded with the yellowish-brown granules seen in the sections treated only with Müller's fluid. The remaining cells showed a diffuse olive-green homogeneous cytoplasm rather than a granular appearance. Fairly numerous rather cleft-like irregular spaces (the vacuolated spaces) were seen in the

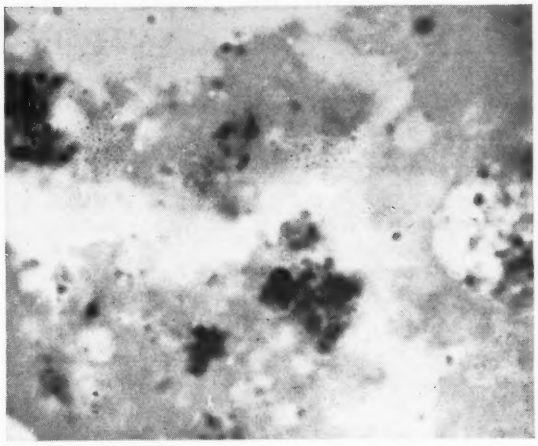


FIG. 191.—*Case* 1. Vacuolated space containing disintegrating tumour cells with liberation of granules. Sevki's modification of Schmorl's method. (× 900.)

section; the fluid in these also showed a similar but rather fainter greenish colour. This faint greenish tint was also evident in the serum in the lumen of the capillaries and also in that in the veins (*Fig.* 190). Sections stained by Mallory's method showed a rather indistinct finely granular cytoplasm in some of the tumour cells, the granules staining orange-brown. No fat was demonstrated in frozen sections stained by Sudan III, or glycogen in tissue fixed in alcohol or Bouin and stained by Best's carmine. In sections stained by a modification

of Bielschowsky's method no reticulin was found lining the sinusoidal channels or the vacuolated spaces, the lining consisting only of tumour cells. It is possible that the vacuolated spaces are an artefact resulting from the drastic fixation in the Müller's fluid causing separation of the tumour cells in the region of the blood-sinuses.

FIG. 192.—*Case* 1. Vacuolated space in the wall of which a large tumour cell with vacuole: in the lumen a disintegrating tumour cell with granules. Sevki's modification of Schmorl's method. (× 900.)

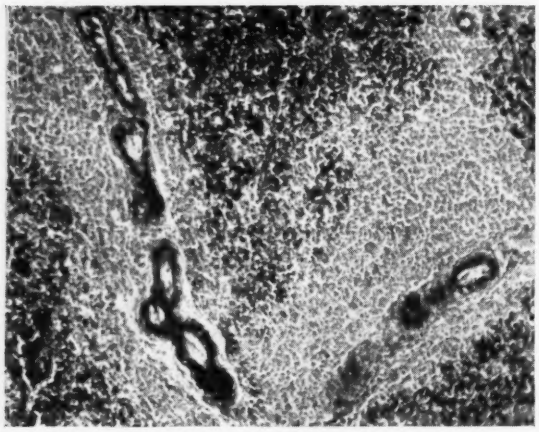


FIG. 193.—*Case*. 1. Hyaline thickening of arterioles in spleen. Gallego's modification of Mallory. (× 100.)

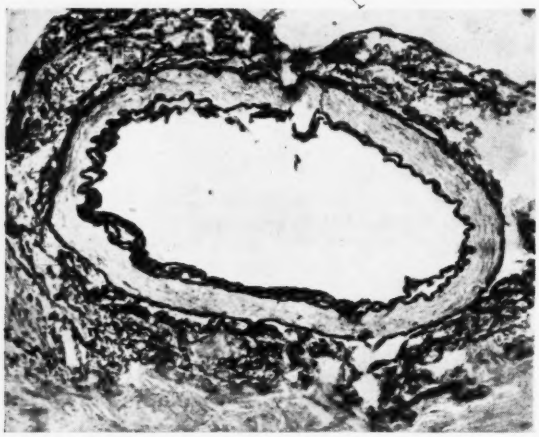


FIG. 194.—*Case* 1. Arcuate vessel of kidney showing thickened intima and reduplication of internal elastic lamina. Weigert's elastic stain. (× 75.)

They were only present in tissue fixed by this method. These vacuolated spaces, however, contained cells with granules and various stages of disintegration of the cells were noted allowing the escape of the granules (*Fig.* 191). This may be the method by which the pressor substance is liberated and may explain the green-coloured fluid in the spaces. An interesting finding, and one already noted by Howard and Barker (1937), was the occurrence of large vacuoles in some of the cells lining the spaces, but the material in the vacuoles could not be stained by

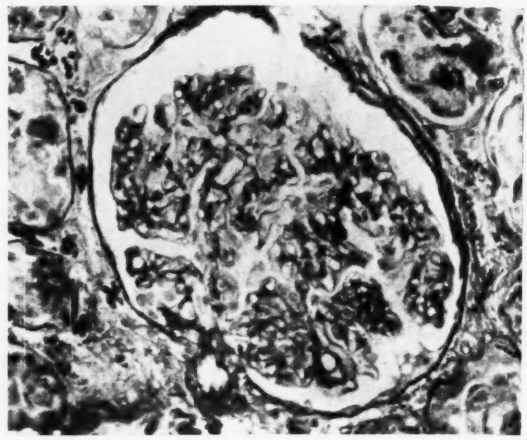


FIG. 195.—*Case* 1. Glomerulus showing thickening of walls of capillaries and of Bowman's capsule. Increase of interstitial tissue outside glomerulus and between tubules. Mallory. (× 200.)

any of the methods we used (*Fig.* 192). These vacuoles may, however, have formed after liberation of the pressor substance.

Detailed microscopical study of the organs and tissues taken post mortem revealed some interesting changes. The arterioles in the spleen, both in the pulp and in the

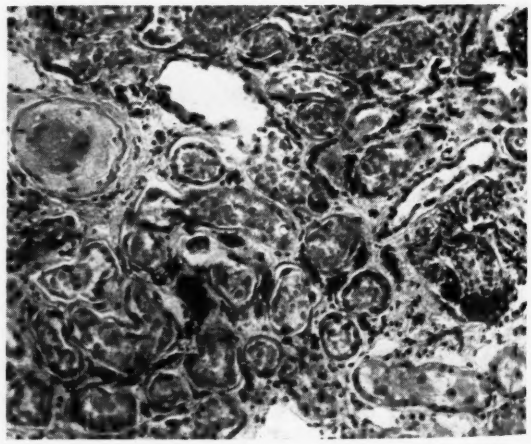


FIG. 196.—*Case* 1. Kidney: sclerosed glomerulus on left; on right adhesion of tuft to capsule. Some increase of interstitial tissue. H. and E. (× 150.)

Malpighian bodies, showed hyaline thickening (*Fig.* 193). The arcuate vessels of the kidneys exhibited distinct fibrosis of the middle coats in addition to some increase in thickness of the intima and splitting of the internal elastic lamina (*Fig.* 194). The walls of the afferent arterioles to the glomeruli were partly hyalinized, the lumen being narrowed. The glomerular capillaries were thickened, staining deep blue with Mallory (*Fig.* 195): a few were completely fibrosed, and in others there was

some adhesion of the tuft to the capsule (*Fig.* 196). The interstitial tissue of the kidney was slightly increased, particularly around the glomeruli, causing thickening of the basement membrane of Bowman's capsule. In the liver small deposits of bile-pigment were present in some of the cells and the walls of the hepatic arteries showed slight hyalinization.

In the pancreas the islet tissue was definitely hyperplastic and the islets were more numerous, often four to five being found in the same high-power field (*Fig.* 197).

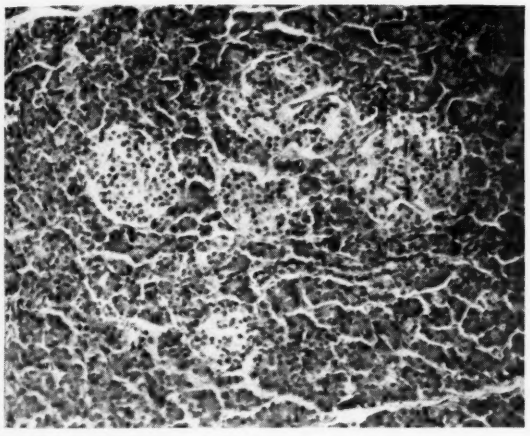


FIG. 197.—*Case* 1. Pancreas ; five hyperplastic islets in one field. H. and E. (× 100.)

An attempt was made to stain the α and β granules in the cells of the islets, but this failed owing to the patient having died 24 hours before autopsy. In the pituitary the eosinophil cells appeared increased, but when a count was made the proportion of these cells to the basophil and chromophobe cells was normal. The chromaffin and the cortical tissue of the suprarenal on the side opposite to that on which the tumour was found appeared normal. All the other organs were examined, but apart from slight congestion no gross lesion was found.

Case 2.—

CLINICAL FINDINGS.—The patient, a housewife, aged 37, was first seen on May 5, 1944. She complained of frequent attacks of weakness and faintness accompanied by many other distressing symptoms such as severe headaches, giddiness, buzzing in the ears, pain over the front of the chest and down both arms, palpitation, a choking sensation, and nausea. These attacks, which had troubled her for at least eighteen months, were usually brought on by exertion or excitement. They steadily increased in frequency and severity, ultimately occurring as often as six times a day, even while she was resting in bed. The duration of each attack varied from five minutes to one hour. She stated that she often felt giddy when lying on her left side. There were no relevant features in the past or family histories.

On examination it was noted that she was a woman of average nutrition but of rather pale complexion. The heart, lungs, abdomen, and nervous system, including the ocular fundi, revealed no abnormality, but the blood-pressure readings were found to be abnormally high (220/115 mm. Hg). It was decided to send her to hospital for further investigation, and she was admitted four days later (May 9).

On the day of admission the urine was found to contain albumin (1 part Esbach), but the blood-pressure reading was now 148/78 mm. Hg. On the following day blood-urea estimation was found to be 101 mg. per cent. While in hospital she had frequent attacks of precordial pain, choking, and severe headaches, and it was noted that these attacks were accompanied by a considerable increase in the blood-pressure : the reading was on an average 265/155 mm. Hg, but at times the systolic could not be estimated with the ordinary sphygmomanometer registering a maximum of 300 mm. Hg. On June 9 the albuminuria was reduced to a mere trace, and blood-urea was 42 mg. per cent.

INVESTIGATIONS.—Intravenous pyelography showed ptosis of the right kidney, but neither kidney nor urinary tract was abnormal in size or form. During a hypertensive attack the serum-potassium was 33·5 mg. per cent (B.P. 265/155 mm. Hg) ; during a normal period 24·6 mg. per cent (B.P. 120/70 mm. Hg). Electrocardiogram : during a normal period, in Leads II and III, S wave increased, large P wave, and elevation of R–T segment. During a hypertensive attack, similar changes were present in S and F waves, but no elevation of R–T.

OPERATION (July 20).—No trouble was encountered in anæsthetizing this patient, who had been heavily premedicated. Pentothal intravenously was followed by endotracheal gas and ether.

A lumbar extraperitoneal incision was made, extending up to the eleventh rib. On opening Gerota's fascia a rounded tumour was seen above and somewhat medial to the upper pole of the right kidney. Before attempting to free this tumour the last rib was resected, thus affording an excellent exposure. The growth was cleared by gentle gauze dissection and ligatures were applied to two groups of small vessels, one of which ascended from the region of the renal pedicle and the other which descended from the diaphragm. The tumour was now drawn up gently into the wound and a third group of vessels which entered its medial aspect was clamped and ligated. The bed left by the removal of the tumour showed slight oozing, which was easily controlled by light packing.

Throughout the operation the patient's general condition was excellent, though her pulse-rate rose from 100 to 120 near the end. The systolic blood-pressure prior to operation was 160 mm. Hg. It rose to 180 soon after the incision had been made and remained at this level until the tumour was handled, when it reached 220 only to fall sharply to 120 when the main pedicle had been clamped. On the patient's return to the ward the pressure fell still further to 80, but responded to 5 minims of adrenaline given every half-hour for 24 hours, followed by 5 minims hourly for a further 24 hours. In the 48 hours, a total of 180 minims of adrenaline was administered. Thereafter 1½ gr. of ephedrine was given at intervals of 12 hours for two days. Eucortone (1 c.c.) was also administered six-hourly for two days as a precaution. Four hours after operation the systolic pressure was 100 and by the evening it had reached 120–130, at which level it remained throughout her smooth convalescence, which was thereafter uneventful.

Some six months later, when the patient reported, the blood-pressure was normal and she had had no further paroxysms. She was very well and was able to perform all her household duties.

PATHOLOGICAL FINDINGS.—The tumour in this case, received one hour after removal, when fresh measured 6·5 cm. long, 5·5 cm. broad, and 3·5 cm. thick, and weighed 70 g. It was roughly oval in shape and had a thick fibrous capsule in which blood-vessels were prominent. The cut surface had a pinkish-white colour, with a few small areas of recent hæmorrhage. Portions were fixed as in the first case and a similar brown colour developed after fixation. In hæmatoxylin and eosin preparations the cells were much better preserved than in the first case owing to the specimen having been fixed an hour after excision. Small remnants of suprarenal cortex were still present outside the thick fibrous capsule of the tumour. The tumour was very vascular and there were many small hæmorrhages in relation to the sinusoids and capillaries (*Fig.* 198). The cells were similar to

those in the first case, though more irregular in size and in shape and much better defined. The cytoplasm was, however, more granular and had a distinct foamy appearance (*Fig.* 199). The fine bluish cytoplasmic granules noted in the first case were more numerous and clumps of small dark-brownish granules which did not give an iron reaction were present in some cells and also lying free in the centre of masses of cells. Some of the cells had more than one nucleus, three being the maximum; some of the nuclei were very irregular in shape and rather large and pyknotic. Mitosis was also more frequent than in the first case. A rather unusual finding was the presence of fairly large numbers of the tumour cells in the lumen of thick-walled veins (*Fig.* 200), though, as in the first case, some tumour cells were seen lying free in the sinusoids. The staining reaction with Mallory corresponded with that in the first case, the outlines of the cells being sharply defined, giving the appearance of an irregular mosaic (*Fig.* 201). In sections stained by the modification of Sevki's method fine abundant olive-green granules were observed in most of the cells, though those next the sinusoids were more vacuolated and less granular (*Fig.* 202). The staining of the granules varied with the degree of differentiation, as when this was overdone the granules stained a yellowish-brown colour, as described by Edward (1937). The tumour cells lying free in the blood-vessels and in the sinusoids also showed granules (*Fig.* 203 A, B). On staining the reticulin the large sinusoids were noted to have no reticular lining, though their continuity with the capillary vessels which had such a lining could sometimes be traced (*Fig.* 204).

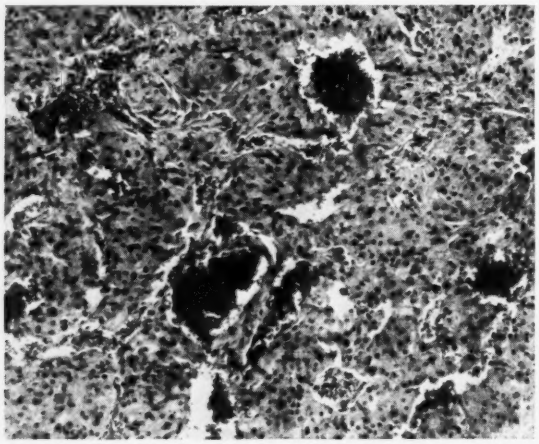


FIG. 198.—*Case* 2. Numerous congested capillaries and sinusoidal spaces with some small hæmorrhages. H. and E. (× 75.)

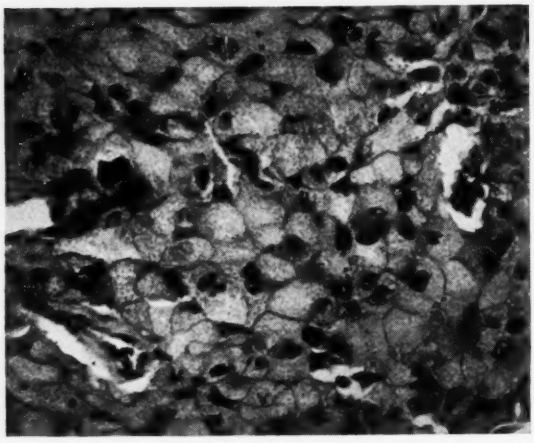


FIG. 199.—*Case* 2. Cells of irregular size and shape, with sharply-defined outline and granular cytoplasm. Modified Masson's trichrome stain. (× 250.)

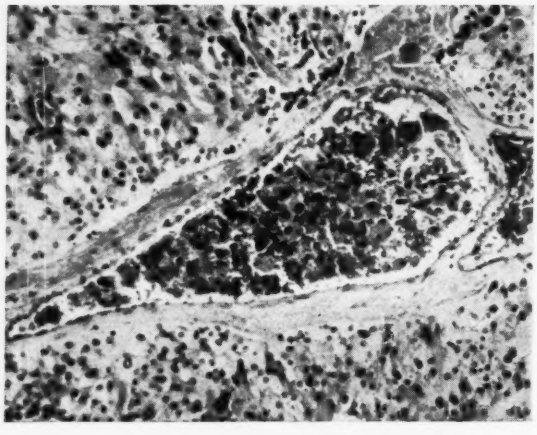


FIG. 200.—*Case* 2.—Tumour cells in lumen of thick-walled vein. H. and E. (× 100.)

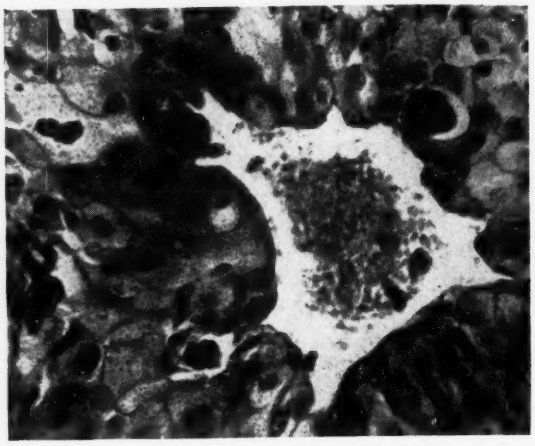


FIG. 201.—*Case* 2. Irregular cells with granular cytoplasm surrounding sinusoidal space giving mosaic appearance. Mallory. (× 250.)

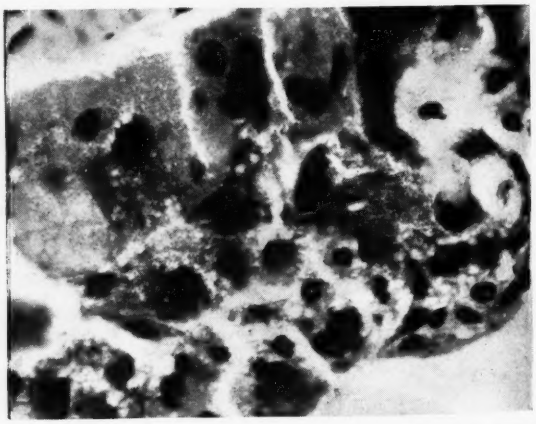
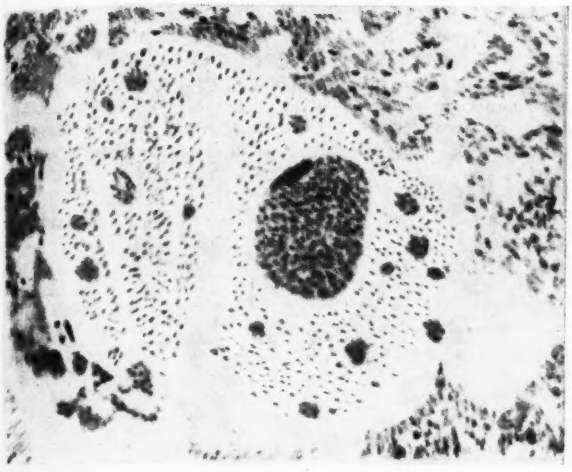
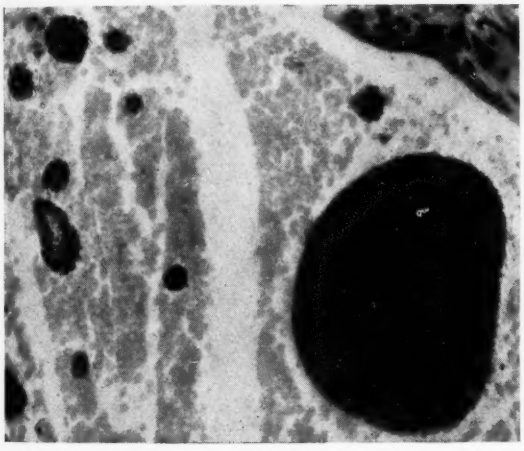


FIG. 202.—*Case* 2. Part of a sinusoidal space at lower right corner: cells immediately adjacent are vacuolated and less granular than those farther away at top left-hand corner. Schmorl's stain. (× 500.)



A



B

FIG. 203.—*Case* 2. A, Sinusoid containing red blood-cells and tumour cells full of pro-adrenaline granules. The cells surrounding the space contain similar granules. Sevki's modification of Schmorl's method. (× 150.) B, A higher power view of cells in sinusoidal space shown in *Fig.* 203 A. These cells are loaded with granules. Sevki's modification of Schmorl's method. (× 500.)

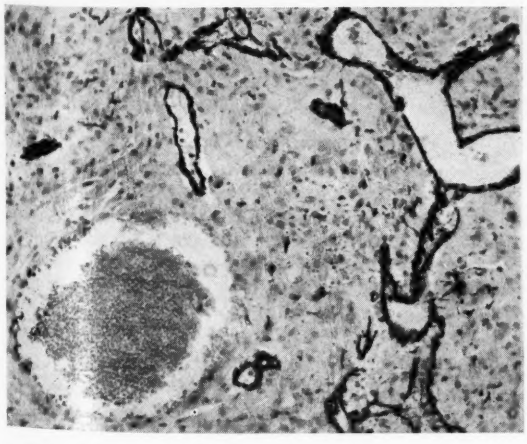


FIG. 204.—*Case* 2. Large sinusoidal space at bottom left corner with no lining of reticulin: capillaries have a reticulin lining. Bielschowsky's method. (× 150.)

Case 3.—

CLINICAL FINDINGS.—The patient, a male aged 39, was admitted to hospital on Oct. 1, 1938. Apart from having to rise at night for almost a year to pass large quantities of pale urine, he had been in good health until three months prior to admission. At that time he became subject to attacks of giddiness when assuming the erect posture after stooping. In some of these attacks there was a temporary loss of power in the legs. Insomnia was a troublesome feature, and his powers of concentration were reduced. Two months after the onset of symptoms he began to complain of severe attacks of pain in the neck radiating to the occipital region; in such an attack "everything went black" and he was forced to grasp some support to prevent himself from falling. The intensity and frequency of these latter attacks increased and were associated with loss of consciousness.

On admission, the patient, a florid type of individual, was restless and fine generalized muscular twitchings were noted. The cardiac dullness was increased to the left and the second aortic sound was accentuated. His eyes were rather prominent and the pupils widely dilated, but they reacted well to light and accommodation. Ophthalmoscopical examination showed some blurring of the margins of the optic discs and arteriosclerotic changes in the vessels. The blood-pressure was 240/130 mg. Hg and the pulse-rate 120 per minute. A trace of albumin was found in the urine and a few red cells were evident in the sediment on microscopical examination. The blood-urea was 43 mg. per cent.

PROGRESS.—A week after admission to hospital the patient died. During this period mental confusion appeared and progressively worsened. He was disorientated, difficult to control, and frequently screamed. Two days before death on Oct. 6 the blood-pressure was 86/56 mm. Hg and 24 hours later 100/30 mm. Hg.

POST-MORTEM FINDINGS.—The post-mortem was performed 12 hours after death. The heart (620 g.) showed great hypertrophy and enlargement of the left ventricle: no valvular lesion was present. The coronary vessels showed slight hypertensive sclerosis, as also did the main branches of the aorta. No lesion was noted in the lungs, liver, or spleen apart from some recent venous congestion. The kidneys (right 270 g.; left 105 g.) showed irregularity of the cortical markings and some yellowish and reddish mottling of the cut surface. There were no hæmorrhages, but the branches of the renal arteries in the substance of the organ were prominent. The capsule stripped easily from both organs, leaving a smooth surface. No reason was observed for the greater size of the right kidney. The brain showed no lesion: the arteries at the base were slightly sclerotic.

The right suprarenal was normal: in the upper pole of the left a small, fairly sharply defined greyish-white tumour, 1 cm. in diameter, was present in the medulla.

HISTOLOGICAL FINDINGS.—In hæmatoxylin-stained sections the tumour cells showed much post-mortem autolysis, the outlines of the cells being indistinct and the nuclei showing pyknosis and chromatolysis. This marked autolysis such a short time after death was an interesting and noteworthy feature. The cells had a more foamy and vacuolated cytoplasm than in either of the two preceding cases. The same alveolar arrangement was present but the alveoli were smaller, containing ten to twenty cells. The cells were more uniform in size and the nuclei more regular in appearance than in the first two cases. A rather thin fibrous capsule was present and this ran through and included part of the zona reticularis at places. On staining by Schmorl's modification of Giemsa and by Sevki's method, only some of the cells showed the olive-green granules, most of the cells having a diffuse greenish tint in their cytoplasm, suggesting that on account of post-mortem autolysis the granules had dissolved in the cytoplasm.

Case 4.—

CLINICAL FINDINGS.—The patient, a housewife, 57 years of age, was admitted to hospital on Dec. 6, 1945. She had been well until November, 1945, when she developed a cough and gastro-intestinal symptoms—nausea, vomiting, and diarrhœa. The latter symptoms persisted for three weeks. Her complaints on admission

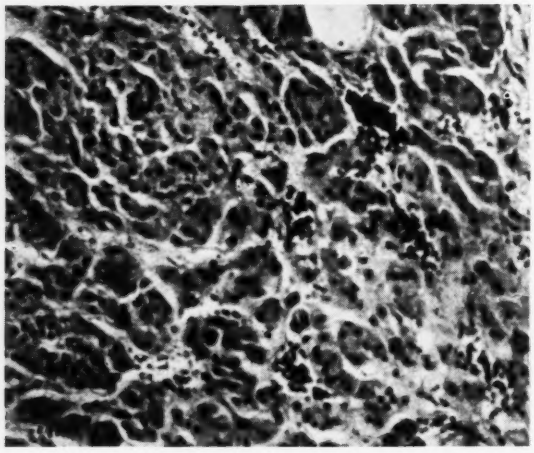


FIG. 205.—*Case* 4. Polyhedral cells arranged in irregular alveoli. H. and E. (× 150.)

were those of general exhaustion and fatigue. There were no relevant features in the past or family history.

Examination showed a well-built woman with clinical evidence of loss of weight. Glossitis was present and the liver was enlarged to 2½ in. below the costal margin. Otherwise no mass or tenderness was detected in the abdomen. Diffuse rhonchi were audible in the chest.

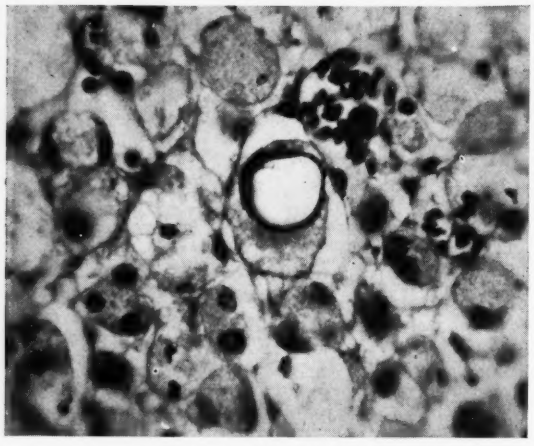


FIG. 206.—*Case* 4. Nucleus of one cell distended by large central vacuole. H. and E. (× 500.)

The other systems did not reveal any abnormal physical signs. The urine contained a cloud of albumin. Hb 74 per cent, R.B.C. 4·12 million, W.B.C. 11,000.

The patient died nine days after admission, during which time pyrexia, tachycardia, and increased respiration-rate were marked. No further localizing features were obtained beyond the presence of an unduly high position of the right diaphragm on radiological examination of the chest. The W.B.C. rose to 28,000 per c.mm. and the blood-urea (Dec. 6) was 101 mg. per cent. Records of the blood-pressure taken on six separate days showed a systolic varying between 105 and 85 mm. Hg and a diastolic between 65 and 50 mm. Hg.

POST-MORTEM FINDINGS.—The autopsy was performed five hours after death. The heart weighed 250 g. and appeared normal. A large chronic abscess occupied most of the right lobe of the liver: from the abscess were isolated *B. coli*, *Staph. pyogenes*, and enterococcus. The gall-bladder was thick, fibrous, and contracted around a faceted gall-stone. The kidneys (right 200 g.; left 205 g.) appeared normal. A chronic periostitis was present in the neck of the right femur.

In the right suprarenal a well-encapsulated tumour, 3 cm. long, 2 cm. broad, and 0·5 cm. in thickness was found. The growth, which was in the medulla of the gland, was encircled with cortical tissue, had a light-brownish colour, and was rather soft in consistence. The left suprarenal appeared normal.

HISTOLOGICAL FINDINGS.—Tissues were fixed as in the previous cases, but in addition some were preserved in a solution composed of equal parts of 5 per cent potassium bichromate and 10 per cent neutral formalin. As will be observed later, this fixative gave much better results with stains used to demonstrate the chromaffin

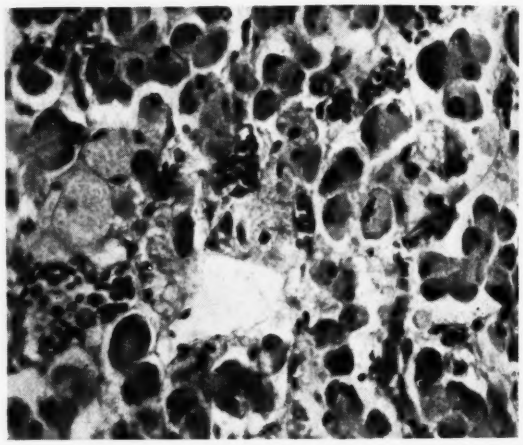


FIG. 207.—*Case* 4. Cells resembling ganglion cells around a sinusoidal space. H. and E. (× 250.)

granules. In the various fixatives the portions of the growth fairly quickly became brownish in colour.

Tissue stained by hæmatoxylin and eosin showed fairly well-defined cells, some being rounded or oval, others more elongated and polyhedral and arranged in irregular alveoli (*Fig.* 205). Most of the cells had a granular cytoplasm, but in some this was foamy and in others vacuolated. The last may have been due to post-mortem autolysis. The nucleus again was vesicular, with one or more nucleoli. Some cells had two or three nuclei. Sometimes the nucleus was distended by a large central vacuole, giving a fairly typical signet-ring appearance, as originally described by Eisenberg and Wallerstein (1932) (*Fig.* 206). Some of the cells closely resembled ganglion cells similar to those seen in a ganglio-neuroma (*Fig.* 207). Most cells, including those resembling ganglion cells, contained fine brownish granules: these did not give a reaction for iron. Numerous fine capillaries were present in the growth as well as a few sinusoidal spaces. A fairly thick fibrous capsule in which small nests of cortical cells were present separated the tumour from the encircling cortical tissue (*Fig.* 208). Mallory's stain demonstrated more clearly the granular cytoplasm and the alveolar nature of the growth. The alveoli were small, containing from one to five cells. In this case only did silver staining show reticulin lining the sinusoidal spaces. In sections stained by the modification of Sevki's stain after the formol-bichromate fixation described above, abundant rather dark-green granules

were seen in cells, particularly those in the vicinity of the blood-vessels (*Fig.* 209). These granules were much coarser and more sharply defined than in any of the previous cases: this may have been due to the different method of fixation adopted in this case or to the fact that the tumour was not physiologically active.

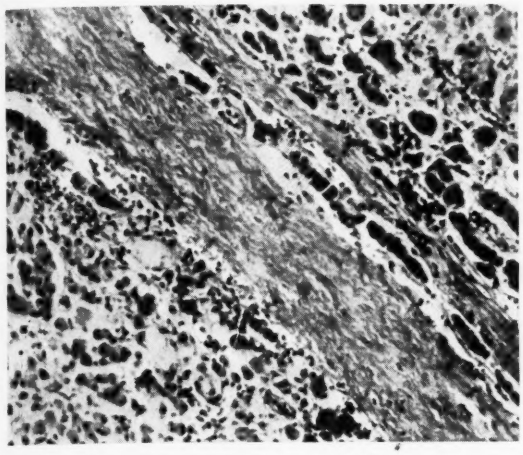


FIG. 208.—*Case* 4. Tumour to left and below separated from cortex to right and above by thick fibrous tissue capsule. H. and E. (× 100.)

In the kidneys the walls of the glomerular capillaries were slightly thickened, particularly the afferent arteriole, as it entered the tuft. There was a slight increase in the interstitial tissue, particularly around the glomeruli. A few of the glomeruli were completely fibrosed and the interlobular arteries showed some fibrosis of the media, thickening of the intima, and splitting of the internal

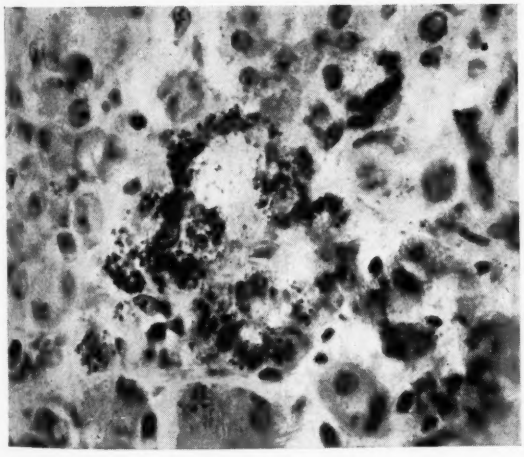


FIG. 209.—*Case* 4. Abundant dark coarse granules in cells. These granules stained dark green by Sevki's modification of Schmorl's method after formol bichromate fixation. (× 500.)

elastic lamina. On account of the patient's age it is doubtful if these changes were due to the effects of the tumour. In the spleen the walls of the capillaries, both in the pulp and in the Malpighian bodies, showed slight hyalinization, as also did the branches of the hepatic artery within the liver.

Case 5.—

CLINICAL HISTORY.—The patient, a male aged 73, was admitted to a surgical ward with a history of incontinence of urine of six months' duration. He was well built, had evidently lost some weight recently, and appeared extremely ill. He was mentally confused and no details of his illness could be obtained. Lips and ears were cyanosed and breathing was rapid, shallow, and distressed, so that he had to be propped up in bed. His tongue was very dry, cracked, and heavily coated. There was a moderate amount of œdema over the sacrum. Investigation of bladder function revealed no retention, and only a few cubic centimetres of residual urine were obtained on catheterization. Urine contained albumin (0·5 parts Esbach). Rectal examination revealed the prostate to be enlarged and hard and to contain one large nodule in the left lobe. He had a markedly raised blood-pressure, 220/110; the peripheral arteries were thickened and tortuous. Percussion note was impaired at the base of the right lung, where abundant fine and medium crepitations were audible. Blood-urea 71 mg. per cent.

He was treated with abundant fluids, sulphadiazine, and penicillin, but his condition steadily deteriorated. On his transfer to a medical ward six days after admission, temperature was 100° F., pulse 160 per minute, respirations 50 per minute; more widespread consolidation was evident in the lungs. An electrocardiograph showed changes of nodal tachycardia and bundle-branch block.

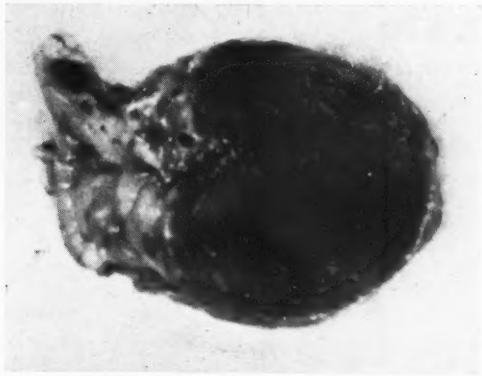


FIG. 210.—*Case* 5. Tumour of right suprarenal surrounded by narrow zone of cortical tissue. (× 2.)

The high pulse-rate was maintained until death occurred three days later. Blood-pressure readings taken on each of the two days prior to death gave readings of 170/110 and 180/110 mm. Hg.

POST-MORTEM FINDINGS.—The post-mortem examination was performed 18 hours after death. The heart, 490 g., was enlarged, chiefly on account of hypertrophy of the left ventricle. The aortic valve was slightly stenosed (8·5 cm. in circumference), due to calcification and adhesion of the cusps. The main pulmonary arteries to the left and right lower lobes were blocked by portions of embolus which had originated from a thrombotic condition in the veins of the legs (posterior tibial and lower part of femoral vein on both sides). Massive infarcts were present in the lower lobes of both lungs. The kidneys (right 120 g.; left 140 g.) showed some adhesion of the capsule to fairly widely scattered depressed areas on their surfaces. The cortex of both organs was slightly irregular in thickness, the markings were fairly regular, and the main branches of the renal arteries in the kidney substance were thickened and there were, in addition, patches of atheroma in their intima. The prostate was slightly enlarged, irregular, and hard, and microscopically a scirrhous cancer was found in its substance. In the middle of the right suprarenal there was a spherical tumour (1·5 cm. in diameter and 8 g. in weight) surrounded by a narrow zone of cortical tissue (*Fig.* 210). The tumour was fleshy in consistence and pale red in colour. The left suprarenal appeared normal.

HISTOLOGICAL FINDINGS.—The tumour in the suprarenal had similar characters to those already described,

but showed a more marked alveolar arrangement than in any of the other cases (*Figs.* 211, 212), each alveolus being outlined by a well-marked layer of reticulum. The growth was only partly encapsulated by a narrow zone of fibrous tissue which ran through the zona reticularis of the gland. There was a well-developed vascularity but

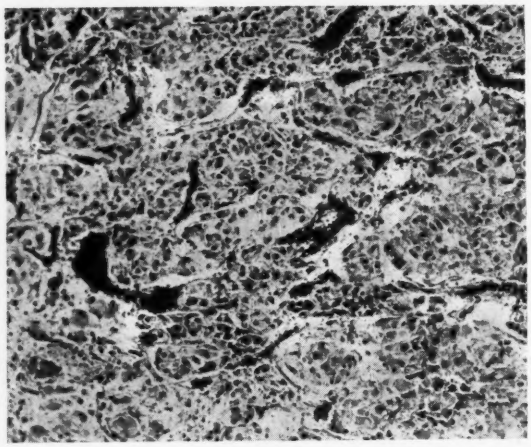


FIG. 211.—*Case* 5. Numerous capillaries and sinusoidal spaces: alveolar arrangement of tumour cells. H. and E. (× 75.)

no sinusoidal spaces. No granules were found in the cells in sections stained by Sevki's method, but this was probably due to the length of time elapsing between death and the time of fixation (18 hours). It had been noted that during fixation in Müller's fluid there was only slight darkening of the tumour, in contrast to the very dark colour developing in *Cases* 1–4.

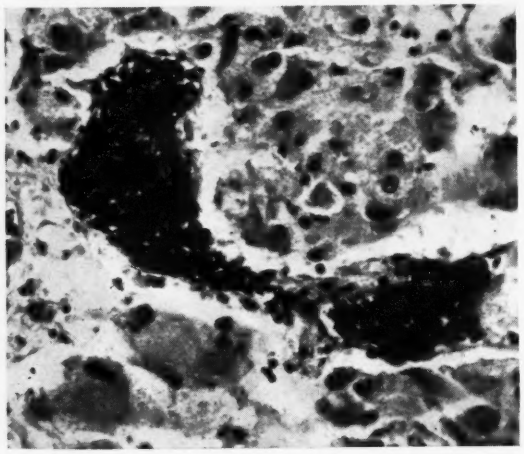


FIG. 212.—*Case* 5. Capillary surrounded by polyhedral cells, with darkly-staining nuclei: cells vary much in size and shape. H. and E. (× 250.)

The kidneys showed some splitting of the internal elastic lamina of the arcuate and interlobar arteries. This, however, may have been due to the age of the patient (73 years) rather than a result of hypertension. Some of the glomeruli were fibrosed, others partly so, but the number thus affected was not large. There was slight patchy irregular overgrowth of fibrous tissue throughout the cortex of the organ.

In the spleen the smaller vessels showed hyaline thickening. A fairly diffuse interlobar fibrosis involved the substance of the pancreas and hyaline change was noted in the walls of the smaller arteries and arterioles. The islets appear larger than normal and more numerous; the latter, however, was possibly due to the interlobar fibrosis causing some contraction of the organ. The liver showed passive congestion only.

Case 6.—

CLINICAL FINDINGS.—The patient, a woman aged 34, was first admitted to hospital on Oct. 17, 1944. Her complaints were those of progressive weakness and breathlessness, which first appeared six months before. In addition she suffered from pain of a dragging nature in the left abdomen; relief was usually obtained by lying down, though at times its severity interfered with her sleep. A month after the onset of these symptoms menstruation, hitherto regular, ceased.

Inspection showed a thin, rather pale woman. The abdomen was somewhat prominent in the left hypochondrium and a firm elastic non-tender rounded mass was palpable in this area. No abnormalities were found on examination of the other systems. The blood-pressure was 128/74 mm. Hg.

A barium enema was performed and the descending colon was shown to be displaced towards the midline. Intravenous pyelography demonstrated deformity of the calices of the left kidney.

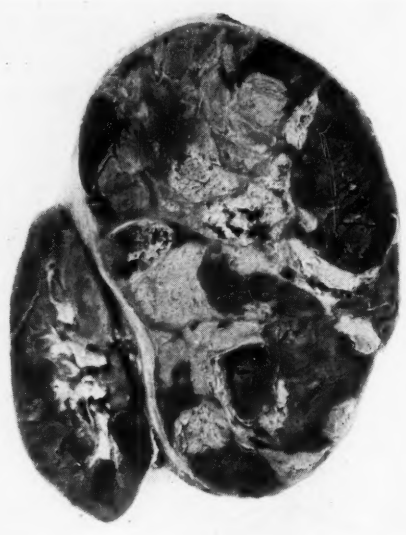


FIG. 213.—*Case* 6. Tumour in thick fibrous capsule showing areas of hæmorrhage and necrosis. Kidney to left and below. (× ½.)

Operation was suggested to the patient, but at her request was postponed till January, 1945. Under gas, oxygen, and ether, Mr. Norman Davidson, through a lumbar incision, exposed the tumour, which with considerable difficulty was delivered into the wound. In places it was adherent to the posterior abdominal wall and the adhesions were tied and sectioned. The kidney was found at the lower pole of the tumour. The kidney pedicle was secured and the kidney and the tumour mass removed. The wound was closed with drainage. After the operation, one pint of plasma and two pints of blood were administered. Convalescence was uneventful. Menstruation returned in February, 1945.

She was examined at frequent intervals, a steady improvement in her physical capacity taking place, until Oct. 6, when she developed marked dyspnœa and physical and radiological examination revealed a large left-sided pleural effusion. Paracentesis thoracis showed the fluid to be blood-stained. On Nov. 30 an artificial pneumothorax was induced, but although the collapse

was satisfactory no further information was obtained. Radiographs of the thoracic and lumbar spine showed no evidence of secondary deposits. In January, 1946, she began to complain of pain in the left hypogastrium and examination showed the upper part of the left rectus muscle to be thickened and firm. The induration extended and by the middle of January a mass in the abdominal wall was palpable. The patient's general condition steadily deteriorated and she died on Feb. 22, 1946. At the time of death the area covered by the tumour included almost the whole of the left side of the abdomen and the medial portion of the right hypochondrium. On the surface of the mass many discrete nodules were evident and were of varied size up to 2 in. in diameter. Post-mortem examination was refused.

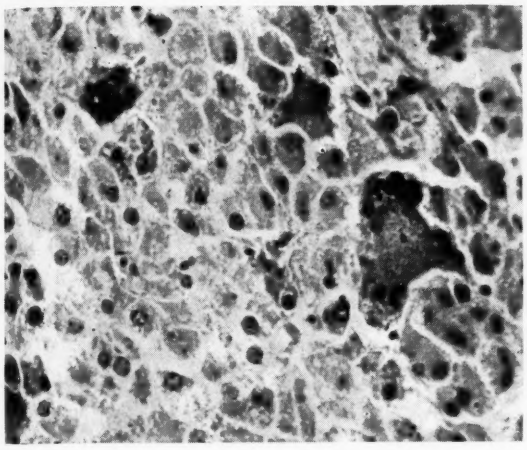


FIG. 214.—*Case* 6. Ill-defined polyhedral cells, with dark nuclei and multinucleated cells. H. and E. (× 250.)

From the time the nature of the growth was recognized until just before death, repeated blood-pressure recordings were made but were all within normal limits.

HISTOLOGICAL FINDINGS.—The specimen was received 24 hours after excision, and the tumour, which was above the right kidney, measured 28 cm. long, 22 cm. broad, and 14 cm. thick, and weighed 1200 g. (*Fig.* 213). It was roughly round in shape and portions of the suprarenal cortex could still be distinguished on the surface of the growth. The tumour, which was contained in a thick fibrous capsule, was quite distinct from the kidney attached below. The growth was much softer than any of the preceding, and the cut surface showed large yellowish-green areas of necrosis and areas of hæmorrhage. Portions of the growth were fixed as formerly, but it was observed that the brownish colour noted in the other cases did not develop in any of the fixatives, including those containing bichromate.

In sections stained with hæmatoxylin and eosin the cells were not as sharply defined as in the first two cases, but had for the most part the same rather elongated polyhedral character. The eosinophil cytoplasm was slightly granular, and the nuclei were smaller and darker than in any of the other cases and less vesicular in character. Mitoses were readily found in most fields examined. The alveoli were large, the fibrous tissue surrounding them being rather fine. Cells with many nuclei were present throughout the section, particularly in the neighbourhood of areas of necrosis (*Fig.* 214). As in *Case* 2, tumour cells were found in some of the blood-vessels (*Fig.* 215), which for the most part were numerous fine capillaries, the tumour thus being very vascular; sinusoidal spaces were, however, scanty. Throughout the growth there were numerous areas of necrosis and hæmorrhage. Tissue fixed in Müller's fluid and stained by Schmorl's, Giemsa, or Sevki's method showed no granules, nor was any greenish colour noted in the cells. This may have been due to the length of time elapsing between the operation and the fixation of the tumour. Silver staining revealed the same arrangement of the reticulin as in the other cases. No fat was observed in any of the tumour cells, though some was observed in the necrotic tissue. A fairly thick capsule surrounded the whole growth.

The kidney, which was attached to the neoplasm, showed some thickening of the basement membrane of the glomerular capillaries and slight increase of the interstitial tissue, particularly in relation to the glomeruli in sections stained by Mallory. In tissue stained for elastic tissue some reduplication of the internal elastic lamina of the arcuate vessels was noted (*Fig.* 216).

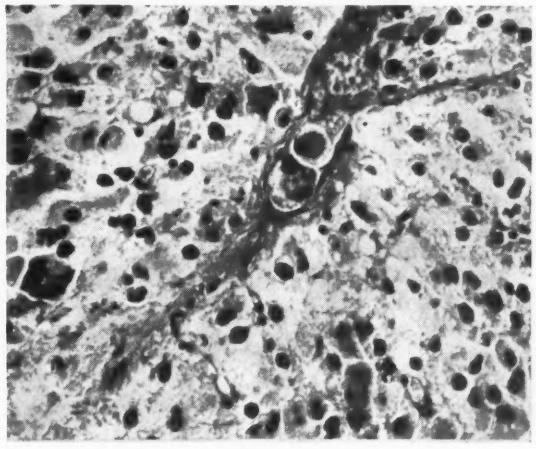


FIG. 215.—*Case* 6. Capillary surrounded by tumour cells: several tumour cells in lumen of vessel. H. and E. (× 250.)

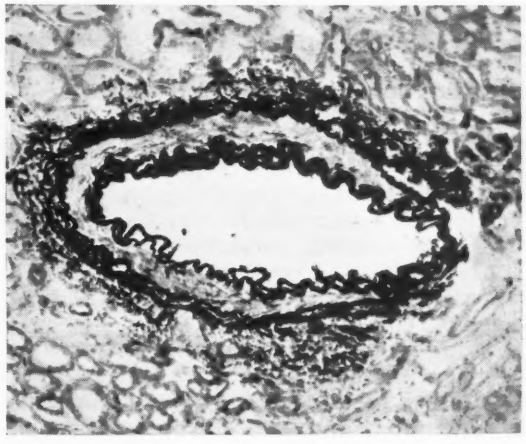


FIG. 216.—*Case* 6. Arcuate vessel of kidney, showing thickening and splitting of internal elastic lamina. Weigert's elastic stain. (× 250.)

Extraction of the Tumour.—Portions of the tumour were extracted with N/10 HCl according to the method described by Kirshbaum and Balkin (1942), but no adrenaline reaction was given with ferric chloride or Folin's 1 per cent phosphomolybdic acid. As these tests were negative, no biological assay was made.

DISCUSSION

CLINICAL

It is obvious from our case reports that the clinical manifestations of phæochromocytoma vary much.

The cases described in this paper fall into four fairly well-defined clinical groups. The first group, which consists of *Cases* 1 and 2, showed the typical adrenal-sympathetic syndrome described by McKeith (1944). *Case* 3, in which persistent hypertension was possibly the chief feature, constitutes the second group, while *Cases* 4 and 5, which were asymptomatic, the third group. The only malignant case in the series completes the fourth group (*Case* 6).

Group I. Adrenal-sympathetic Syndrome (*Cases* 1, 2).—In this group the symptoms are plainly recognizable, the first clear description being give in 1922 by Labbé, Tinel, and Doumer. In our cases the attacks had extended over short periods, though they may extend over years, Allen (1940) having recorded a case of at least sixteen years' duration. The symptoms can be explained by the excessive and intermittent excretion of adrenaline into the blood-stream. Beer et al. (1937) and Strombeck and Hedberg (1939) have demonstrated an excess of adrenaline-like pressor substance in the blood. In *Cases* 1 and 2 it was shown histologically that abundant pro-adrenaline granules were present in the cells of the growth, and these granules were observed passing from the tumour cells into the capillaries. Unfortunately, in both cases it was not possible to confirm the nature of these granules by biological tests. The tumours in both were of moderate size, one weighing 86 g. and the other 70 g., whereas those falling into the asymptomatic group were much smaller.

The cardiovascular disturbances are most striking. In both of our cases the systolic pressure was raised (260 mm. in *Case* 1, and over 300 mm. in *Case* 2); the diastolic pressure was correspondingly elevated. Associated with this there is a marked and widespread vasoconstriction, the pulse often being thin and sometimes impalpable. Indeed, oscillometric recordings show a pronounced fall in the distal portions of the extremities, and in severe cases it may not be possible to obtain a pressure reading because of the absence of peripheral vascular pulsation. In *Case* 1 the effect of this hypertension was evident in the hypertrophy of the left ventricle and the hypertensive arterio- and arteriolo-sclerosis found post mortem. Other cardiovascular symptoms have been noted by various authors; Howard and Barker (1937) in an analysis of 18 cases found a marked distension of the neck veins in 5. Pallor and coldness of the face and of the extremities are commonly present, but it is to be noted that while the skin temperature falls, the body temperature, as shown by rectal readings, usually rises. The angiospasm of the extremities and of the tip of the nose may be confused with signs of Raynaud's disease. The heart rate may be unaltered, but usually there is a tachycardia present, or a slow forceful cardiac impulse. Symptoms referable to the cardiovascular system are sometimes observed, including palpitations, precordial pain, pain of an anginoid nature, and a feeling of constriction around the chest. Changes in the electrocardiograph have frequently been reported, but these show no consistent or distinctive pattern. Many other subjective experiences may be described by the patient, who may find difficulty in analysing adequately the peculiar sensations. In this respect, emphasis must be placed on the similarity between them and those commonly found in subjects with functional nervous disorders. A sinking feeling in the abdomen, numbness in the extremities, choking sensations, dizziness, feelings of anxiety, paræsthesia, a sensation of heat around the face, and sweating have been variously described in published reports. Headaches are frequent and may be very severe, being referred to as of a 'pounding' character. Nausea and vomiting, especially if the seizure succeeds a meal, are frequent; diarrhœa is less common. Lacrimation and dilatation of the pupils have been described.

During an attack, the urinary output may fall, and albumin, red blood-cells, and casts have occasionally been found. In none of our cases was the urine examined at this time, though in *Case* 2 albumin was present in the intervals between the attacks. In both cases, transient nitrogen retention occurred in *Case* 1 after, and in *Case* 2 before, operation; blood-urea levels as high as 150 mg. per cent, however, have been reported (McKeith, 1944). The blood-sugar tends to rise in parallel with the rise in blood-pressure, and thus elevated blood-sugar levels and resulting glycosuria are common, though such was not observed in either of the cases in this group. This may have been due to the fact that the blood-sugar was not estimated in either case during an attack. The finding of hyperplasia of the islet tissue in the pancreas post mortem in *Case* 1 is of interest, and may help to explain the normal blood-sugar curve, as there may have been periods of hyperinsulinæmia. The reason for this hyperplasia of islet tissue cannot solely be explained by the hypersecretion of adrenaline.

Boman and Wells (1937) drew attention to the possible value of a rise in serum-potassium as an aid to diagnosis, as in our *Case* 2, where the serum-potassium rose to 33·5 mg. per 100 c.c. during a hypertensive attack from 24·6 in the interval between the attacks; in *Case* 1 we have no observations on this point.

There is a wide range in the duration of the paroxysm, which may last for a few minutes as in *Case* 1, though as the disease progresses they tend to become longer as in *Case* 2, and have even lasted for as long as 36 hours, as reported by Hyman and Mencher (1943). In this respect it should be realized that the fleeting duration of an attack may fail to draw attention to the underlying condition. These minor attacks, as well as localized forms, are particularly liable to be disregarded or confused with other conditions. The localized form tends to produce symptoms referable to a particular system, so that the generalized nature of the disturbance may be masked. Examples of these are afforded by the patient of Labbé et al. (1922), who suffered from daily bouts of vomiting, and by the case of Shipley (1929), in which vomiting and diarrhœa were transient symptoms; similarly anginal attacks, precordial pain, transient periods of fatigue, and lassitude may be the salient features.

Following the attack a feeling of weakness and prostration is commonly experienced, especially if the attack has been of long duration. The fall in blood-pressure is usually fairly rapid, as in our *Case* 2, and sometimes it may reach subnormal levels.

Between the attacks the patient usually feels well, though some loss of weight and mild anæmia have been reported. The blood-pressure readings are as a rule normal, but there is a tendency for persistent hypertension to develop with the increasing duration of the illness, as in *Case* 1. Of the 76 cases of paroxysmal hypertension noted in *Table IV*, accurate blood-pressure readings were available in 53, and of these 20 showed a persistent raised pressure, rising further with paroxysms. These figures differ from those recorded by Green (1946), but this is due to our criterion of what constitutes hypertension differing from that of this author. We considered hypertension to be present when the systolic pressure was 140 mm. or over, and the diastolic 100 mm. or over. Green (1946), on the other hand, considered the hypertension to be chronic when the interval blood-pressure was either (*a*) 140 mm. systolic and 90 mm. diastolic, or (*b*) 95 mm. diastolic. Thus this group may require to be further subdivided into (*a*) those in whom the blood-pressure in the intervals is about normal, and (*b*) those in whom the interval blood-pressure is persistently raised; in both there are the superadded paroxysms which are more frequent in Group (*b*). It should be noted that Group (*a*) tends to merge into Group (*b*) as time passes. By the time the patient is first studied, the basal blood-pressure may be at a persistently high level and paroxysms may be difficult to observe. The careful analysis of the history in such cases, however, frequently suggests the presence of paroxysms of the adrenal sympathetic type.

Individual peculiarities are found in the factors responsible for the precipitation of an attack, but many of these refer to stimuli which produce a sympathetic stimulating response. Pain, exercise, and emotional disturbances are among the commonest. In *Case* 1 attacks were sometimes brought on by exercise, though they also occurred when the patient was sleeping and may have been due to some psychical disturbance due to service conditions; in *Case* 2 exercise and excitement were at first factors initiating an attack, though later attacks occurred even at rest. Either flexion or extension of the affected side may lead to an attack and thus postural changes are not of much value in determining the side of the tumour. In only 50 per cent of cases are definite precipitating factors detectable. Pressure on the upper abdominal quadrant in which the tumour is situated (McKenzie and McEachern, 1938), lying on the side of the tumour, hyperventilation, the cold pressor test, and pressure over the carotid sinus have all been known to produce attacks. The induction of attacks by the intravenous injection of small quantities of histamine (Roth and Kvale, 1945) is worthy of note; this procedure may with experience prove useful as a test for the presence of phæochromocytoma. Attacks are common under anæsthesia and with operations even of a minor type. A fatal paroxysm after drinking 1500 c.c. of water has been reported (Howard and Barker, 1937).

While the usual case tends to show a steady increase, both in the frequency and severity of paroxysms, long intervals of freedom may occur; Shipley (1929) and Pincoff (1929) reported a period lasting four years and Hamilton (1940) one of ten years. This irregularity in the occurrence of paroxysms adds further difficulty to diagnosis. In *Case* 1, had major attacks not been witnessed, great difficulty would have been experienced in interpreting the minor manifestations which took place during the succeeding months of observation. *Case* 2 further emphasizes the diagnostic difficulties, for she had been examined by numerous consultants before admission to hospital, the most common diagnosis being that of a neurosis.

Difficulty may be experienced in differentiating the condition from the hypertensive crises of essential hypertension, though cerebral symptoms are usually more prominent in the latter. Hypoglycæmic attacks may present a similar symptomatology to that of a paroxysm; the blood-sugar and blood-pressure values are, however, distinguishing features. Tumours in the region of the third ventricle or hypothalamus, because of their particular locality, may produce somewhat similar hypertensive attacks referable to excitation of the autonomic nervous system. An increased metabolic rate is not infrequent in cases of phæochromocytoma and confusion with hyperthyroidism may therefore result. In one of the cases reported by McCullagh and Engel (1942) the hyperthyroidism disappeared following removal of the tumour.

Rodin (1945) attempted to distinguish the fundal changes in phæochromocytoma from those of malignant hypertension, but acknowledged that if the adrenal tumour was not removed the retinal picture characteristic of malignant hypertension might develop. An important observation was the reversibility of the ophthalmoscopic findings as this author described the gradual disappearance of the retinal changes following operation.

Group II. Persistent Hypertension (*Case* 3).—Reference has already been made to the development of persistent hypertension in the later phases of the paroxysmal syndrome. A constantly elevated blood-pressure, however, may exist in the absence of any evidence of pre-existing bouts of paroxysmal hypertension (Kremer, 1936; Rabin, 1929; Thorn Hindle, and Sandmeyer, 1944).

This group may show the clinical features of either benign or malignant hypertension, as in *Case* 3. It should be noted, however, that this patient also displayed some of the features of Group I, viz., severe attacks of pain in the neck, giddiness, and ultimate loss of consciousness, all of which might fall into the category of the adrenal-sympathetic syndrome and may represent the symptoms of a paroxysm. This patient was also under observation for less than a week before death and it is not possible to say more. Cardiac, renal, and cerebral manifestations may appear, and short of finding a local mass in the region of the adrenals there does not seem to be any distinctive features that can differentiate this group from essential hypertension. Indeed *Case* 3 was diagnosed by a physician of long experience as possibly one of malignant hypertension owing to the arteriosclerotic changes in the retina, the cardiovascular disturbances, the high blood-pressure, and urinary changes. The only doubtful feature which was noted at the time was the normal blood-urea. Radiological investigations of the renal tracts in the search for a possible kidney lesion, and the presence of the high blood-pressure together with ophthalmological

changes such as arteriosclerosis of the retinal vessels, hæmorrhage, exudates, and papilloedema might draw attention to the existence of the tumour (Thorn et al., 1944). In *Case* 3, however, the tumour was so small (only 1 cm. in diameter) that no radiological examination would have been of service in diagnosis. In fact, the tumour did not appear from the histological evidence to have existed for long, as the capsule was thin and incomplete. Considering the frequency of essential hypertension and of chronic nephritis it can be readily understood why a case in this group may be misdiagnosed, particularly if it is only under observation for a matter of days, as in our case.

Group III. Asymptomatic (*Cases* 4, 5).—This group of cases is usually disclosed at post-mortem examination (Paul, 1931; Fingerland, 1936; Fein and Carman, 1937). In a review of 135 cases collected from the literature, including our own 6, phæochromocytomata were not associated with hypertension in 16 (11·8 per cent), no mention of hypertension being made in 23. Paroxysmal hypertension was reported in 76, persistent hypertension in only 8, while hypertension was reported but the type not specified in 12. (*Table IV.*) The small

Table IV.—Relationship to Hypertension in 135 Cases*

	Present Series from Literature since 1936, including our own 6 Cases	*Edward* (1937)	*Eisenberg and Wallerstein* (1932)	*Total*
No. of cases	49	34	52	135
Paroxysmal hypertension	39	21	16	76
Persistent hypertension	4	3	1	8
Hypertension only mentioned	0	5	7	12
No mention of hypertension	1	1	21	23
Normal blood-pressure or hypotension	5	4	7	16

* *Tables IV–VI* were compiled from the cases shown in *Tables I–III*

proportion of cases, just over 10 per cent, without hypertension is rather surprising. The reports of some of the earlier cases are somewhat incomplete and the data given might not now be regarded as adequate from the clinical point of view. That such cases do occur, however, is exemplified by *Cases* 4 and 5. No indication was available from the history of these cases, including that obtained from relatives or from clinical examination, as to the presence of a phæochromocytoma. In both cases the tumours were small. In *Case* 4 pro-adrenaline granules were clearly demonstrable though this was not possible in *Case* 5 owing to the length of time between death and autopsy. It might be argued that the tumour in *Case* 5 was secondary to the carcinoma of the prostate. This possibility was recognized at the time, but extensive histological studies showed that the two tumours were different cytologically and that the adrenal tumour corresponded to the other phæochromocytomata described. This association of phæochromocytoma with other neoplasms has been noted by various authors, as commented on by Eisenberg and Wallerstein (1932); no special significance can, however, be attached to this association. In both cases there was post-mortem evidence that hypertension had existed as judged by the arteriosclerotic changes in the vessels of the kidneys and other organs, but whether these changes were due to the hormonal effect of the tumour or to the patient's age (one was 57 and the other 73 years) it was not possible to assess.

Group IV. Malignant (*Case* 6).—This group is discussed later under Pathology.

SURGICAL DIAGNOSIS AND TREATMENT

In deciding the side occupied by the tumour pyelography, either intravenous or ascending, may be of help and was the method of location applied in *Cases* 1 and 2. A large tumour will cause a considerable downward displacement of the kidney on that side, but even a minor degree of renal ptosis may be significant, especially when it is suspected from the clinical evidence that an adrenal tumour is probably present. In *Case* 2, for example, the right kidney was appreciably pushed down by the tumour, while in *Case* 1 a pyelogram taken two months after the initial one did show a slight increase in downward displacement and led to a correct localization. When dealing with smaller tumours or hyperplasia of the adrenal cortex, perirenal insufflation of air has proved to be of great value in our hands, though it was not considered necessary in *Cases* 1 and 2. This diagnostic method is relatively free from risk, but should be used with caution since it may sometimes cause sudden collapse. A further clarification of the radiological picture can sometimes be achieved by carrying out an intravenous pyelogram about two days after the performance of perirenal insufflation. It is doubtful, however, if the smaller tumours such as were found in *Cases* 3, 4, and 5 would be readily located by these methods, as at autopsy no displacement of the kidney was noted.

The pre-operative treatment is of importance. The patient should be as little upset before operation as possible, and heavy premedication should be carried out. In *Case* 1 the importance of this was not fully realized and the fatal ending was largely due to the difficulties encountered by the anæsthetist in dealing with a wakeful and apprehensive patient. In striking contrast to this was the experience with *Case* 2, where the patient was easily anæsthetized, thus making the operation straightforward and the post-operative course singularly uneventful. Patients suffering from adrenal medullary tumours may be treated on similar lines to those having toxic goitres and should be unaware of the time of their operation, otherwise they are liable to develop a hypertensive attack immediately before it.

As regards operation, most surgeons prefer to approach the adrenal through a modified kidney exposure, though Broster (1939) in his earlier work utilized the transpleural route. Young (1937) has stressed the value of seeing both adrenals at the same time, particularly in the adrenogenital syndrome, and has described an approach with the patient prone which makes this possible. We have made use of a renal extraperitoneal exposure in the two patients who were operated upon in the present series, but have had to resect the last rib in both

cases to improve the access and to allow of clearing around the tumour with as little handling of the affected suprarenal as possible. Manipulation of a phæochromocytoma causes a sharp rise of blood-pressure and is to be avoided as far as possible. From the histological evidence it was obvious in *Case* 1 that there had been large excretion of the pro-adrenaline substance, due possibly to anxiety and restlessness of the patient under anæsthesia, as even the serum in the lumen of the capillaries gave a reaction for this substance and granules were noted escaping from cells lining the sinusoidal spaces into the blood-stream. Thus large amounts of adrenaline would be quickly liberated into the circulation, causing shock. Indeed, during operation in *Case* 2, a sharp rise in blood-pressure from 180 mm. to 220 mm. was noted when the tumour was handled, only to fall to 120 mm. when the pedicle was clamped. Thus before handling the growth it is wise if possible to ligate all vessels coming from the tumour so as to prevent as much as possible of the secretion from the adrenal and its tumour gaining access to the general circulation. The upper pole of the kidney can be used as a retractor by pulling it downwards and slightly backwards, thus bringing at the same time the adrenal more into view. The vessels supplying the adrenal are rather friable and require careful ligation. They consist of a main group from the great vessels and accessory and smaller branches from the renal pedicle and from the region of the diaphragm. If they should be torn they are apt to give rise to troublesome bleeding in the depths of the wound.

As regards post-operative treatment it was noted from the histological evidence that the cortex of the affected adrenal was compressed and distributed over a larger area than normal. Thus there would probably be some interference with the secretion of cortical hormone. This effect would be intensified as the result of operation owing to the surgical manipulation in the neighbourhood of the healthy adrenal on the opposite side. These functional disturbances might result in either an excess or diminution of cortical hormone. As yet we have insufficient evidence to support either of these views, though it seems probable that on account of the removal of the tumour-bearing adrenal and the operative interference with the function of the other that there would be, at least, a temporary deficiency in the cortical hormone. This is also the opinion of Engel, Mencher, and Engel (1942). This would require the therapeutic administration of cortical hormone both immediately before and for some time after operation. Our present practice is to give large doses of cortical extract both before and immediately after operation, together with sodium chloride and sodium citrate. In *Case* 2 only a small amount of cortical extract had to be administered after operation. Whether adrenaline should be given or not in addition is a controversial point. It would appear, at least from the histological evidence, that as a result of the operative interference the patient is already well supplied, and further therapeutic administration of adrenaline may intensify the shock due to operation. On the other hand, the sudden withdrawal of the large amounts of adrenaline (from the tumour) to which the patient's tissues have been accustomed may cause collapse due to acute adrenaline insufficiency. In the post-operative medication of their case Thorn at al. (1944) used adrenaline, cortical extract, blood transfusion, and intravenous glucose-saline.

PATHOLOGY

For good cytological studies, particularly the demonstration of the pro-adrenaline granules, fresh tissue is essential. The longer the time elapsing before fixation the less the possibility of staining these granules by any of the specific methods. In our cases granules were clearly demonstrable in post-mortem material up to 5 hours after death, but not after 12, and in operation specimens up to 4 hours after surgical removal. The best fixative was found to be a solution composed of equal parts of 5 per cent bichromate and 10 per cent neutral formalin. Sevki's modification (1934) of Schmorl's Giemsa method gave excellent demonstration of the granules after using this fixative. Müller's fluid, the fixative often employed, was found to be rather drastic and caused artefacts.

When fresh tumour tissue is available biological tests are possible. While such a biological assay is desirable it can only play an ancillary part in diagnosis to a good histological study. Estimation of the blood-adrenaline is of undoubted value, though in none of our cases was this made. This method was used by Strombeck and Hedberg (1939) in their case; the more recent method of Shaw (1938) for the estimation of blood-adrenaline is, however, advisable. The serum-sodium and potassium levels, both during a paroxysm and in the intervals between paroxysms, should also be estimated, as a rise in the serum-potassium in the former is most helpful in diagnosis, as in our second case.

The histological appearance of these tumours is variable. All in the present series were either wholly or partly encapsulated, the capsule for the most part running through the zona reticularis. This is a point of importance as the superficial layers of the cortex, though intact, are compressed by the growth. These cortical cells are thus capable of secretion, though, as previously discussed, the secretion may be abnormal in amount. The tumour cells for the most part are long and polyhedral, though in some of our cases multinucleated cells were also present, and in one case, *Case* 4, some of the cells resembled those seen in ganglioneuroma. This mixture of cells has also been noted by Hedinger (1911), Marchetti (1904), Paul (1931), and Rosenthal and Willis (1936). This is not surprising in view of common ancestry of the cells in the suprarenal medulla from the undifferentiated sympathogonia, and accordingly mixed tumours composed of all types of cells, even including sympathicoblasts (neuroblasts) derived from these primitive cells, may occur. Indeed such tumours have been described by Suzuki (1910), Hedinger (1911), Wahl (1914), Gravier and Bernheim (1924), King (1931), Wahl and Robinson (1943), and McGavack et al. (1942). One of us (Blacklock, 1934) has already suggested a classification of the tumours of the adrenal medulla. This, in view of further experience, may now be extended as follows :—

1. *Sympathicoblastoma* (*All Malignant*).—

a. Undifferentiated, composed only of sympathogonia.

b. Differentiated: (i) Composed of sympathogonia and sympathicosblasts; (ii) Composed of ganglion cells in addition to more primitive cells—Gangliosympathicoblastoma.

2. *Ganglioneuroma.—Generally simple.* Composed only of ganglion cells.

3. *Phæochromocytoma.—Generally simple, but may be malignant.* Composed of adult phæochromocytes, but in the malignant tumours also of more primitive cells, e.g., sympathogonia.

4. *Mixed Tumours* composed of mixtures of any of the above.

All these tumours are very vascular, with the possible exception of the ganglioneuroma. The cells lie in close relation to the capillaries and the blood-sinuses, and thus any hormone formed by the tumour cells readily gains access to the blood-stream, and in the case of phæochromocytomata accounts for the paroxysmal attacks which may be precipitated by slight causes. Further, cells readily escape into the blood-stream even in the simple phæochromocytoma composed only of mature cells as in our *Cases* 1 and 2. The fate of these cells seen in the vessels of the simple tumours is uncertain, though they are probably eventually destroyed in the lung capilliaries as no metastases occurred. The diagnosis of malignancy is, however, on this account rendered difficult. In our *Case* 6 (the only malignant one in the series) the tumour was well encapsulated by thick fibrous tissue. Many of the cells showed the same character as in the simple tumours, but other cells were less well defined and there were numerous multinucleated forms and numerous mitoses. As in the more simple cases, tumour cells were also found in the small capillaries within the neoplasm. Thus in this case the tumour appeared to have been composed of a mixture of adult phæochromocytes and more immature cells, possibly phæochromoblasts. It is these latter cells which probably give rise to the metastases, though this could not be ascertained as no post-mortem examination was possible in this patient. Most of the malignant cases reported have shown a mixture of mature and immature cells.

The commonest site of the tumours in our series was in the right suprarenal (5 cases) and in the left (1 case). This is in accord with the cases reported in the literature as shown in *Table V*. Of our cases 3 occurred in women and 3 in men. In *Table VI* the age and sex distribution of the reported cases and our own cases are shown. It is evident that phæochromocytomata were commoner in the female than in the male, and commonest in the fifth decade, with the fourth and third decades closely following in this order. Indeed, more than half of the cases occurred in the active period of life between 20 and 50. The youngest case reported was in a female child of 16 months (Neff, Tice, Walker, and Ockerblad, 1942) and the oldest in a woman of 82 years (Suzuki, 1910).

Table V.—Site of Occurrence of Phæochromocytoma in a Series of 132 Cases

Site	*No. of Cases*
Right adrenal	64
Left adrenal	39
Both adrenals	13
Mediastinum	1
Not stated	15
Total	132

Note.—3 cases (Fingerland, 1936; Popken, 1936; Bianchedi, 1936) mentioned by Edward (1936) are not included in this series as the original articles could not be consulted.

Table VI.—The Relationship of Sex and Age to the Incidence of Phæochromocytoma

Age	*Males*	*Females*	*Age and Sex not stated*	*Total*
0—10	1	2	—	3
11—20	4	7	—	11
21—30	13	14	—	27
31—40	11	18	—	29
41—50	14	20	—	34
51—60	5	4	—	9
60+	7	7	—	14
	—	—	—	—
	55	72	8	135

Youngest, 1½ years, female (Neff et al., 1942)
Eldest, 82 years, female (Suzuki, 1910)

The photographs are the work of Mr. D. Hay, Senior Technical Assistant, the Department of Pathology, the Royal Infirmary, Glasgow.

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THE THORACO-ABDOMINAL WOUND

SOME OBSERVATIONS ON 20 PERSONAL CASES

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THIS series of 20 soldiers who suffered wounds involving both the pleural and peritoneal cavities, were all operated upon in a Field Surgical Unit with 21 Army Group between June 6, 1944, and March 25, 1945. With the aid of the Army Record Offices I have been able to contact the survivors by letter, and in some instances to examine them.

Of the 20 wounded, 5 died within fourteen days of operation whilst still with the C.C.S. or F.D.S. to which I was attached at the time; the remaining 15 were evacuated fit enough to travel and eventually reached the U.K., where they were treated in E.M.S. hospitals. Now, 18 months later, they are all either back in civilian life or on military duty in the case of 'regulars'.

These results seem to justify the treatment of the chest as well as the abdomen at the primary operation in the Forward Areas.

Three of the casualties with wounds of the right chest involving the diaphragm and liver required forward surgery for continued hæmorrhage. Most wounds in this region could be treated conservatively if there was no evidence of damage to a hollow viscus and no gross destruction of the chest wall. Three more had wounds of the right chest passing through the liver and involving the intestines, with all the signs of peritonitis.

One soldier was wounded in the left loin by a jagged piece of metal which passed through the left kidney, spleen, stomach, and liver to the left lung. The remaining 13 had wounds of the left chest passing through the diaphragm and damaging abdominal viscera.

The gravity of wounds of the liver seems to be unpredictable. Many have been left alone, the foreign body lying in the liver substance and causing no apparent trouble, or passing right through, leaving only small entry and exit wounds which do not bleed. Others have required surgical intervention to stop profuse hæmorrhage. Yet a severe wound causing much liver necrosis (*Case* 3) did not prove fatal, while a small bullet wound which does not even involve the hilum may cause jaundice and eventually death. This jaundice does not usually appear until about ten days after the wound, and the patient may seem to have been making a good recovery during that time.

In civil life I have seen a patient recover though one lobe of her liver sloughed after the right hepatic artery had been ligated. I suspect that infection is the crucial factor which decides between recovery and 'liver death'.

The interval between wounding and operation varied from 3 hours in *Case* 9 to 48 hours in *Case* 17

—a German prisoner who died of peritonitis on the fifth post-operative day.

All patients were first treated by the Field Transfusion Units with transfusions of blood and plasma, administration of morphine, tetanus antitoxin, and penicillin, and redressing of their wounds after a quick general examination. As they recovered from their ambulance journey and shock they were sent to the operating theatre, where as a rule I saw them for the first time. If circumstances permitted a plain anteroposterior radiograph was taken, but often the radiographer was busy with more urgent cases, and if we were working with an F.D.S. there was no X-ray apparatus.

Pre-operative atropine was given and the patient was anæsthetized with ether and oxygen administered through the Oxford vaporizer after induction with pentothal or ethyl chloride. My anæsthetist, Major Kenneth Minto, always passed an endotracheal tube while the orderlies were removing the remains of the patient's clothes and getting rid of dirty blankets. The drip of blood or plasma was kept going and continued later in the ward with glucose-saline or some suitable fluid.

All wounds were inspected and the most serious were dealt with first, minor wounds being dressed under the direction of the anæsthetist while I was operating. The operation site was cleaned with soap and water, or C.T.A.B. when it was available, and then painted with 1–1000 aqueous flavine to colour the cleaned area.

Fifteen patients underwent thoracotomy, lying in the lateral position and held there by a bracket made of padded cramer wire covered with jaconet. The incision was made to excise the entry wound and trim the fractured rib ends, being extended as necessary by intercostal incision, and held open with self-retaining rib spreaders. The lung was first examined and indriven pieces of clothing, muscle, and bone were picked out with forceps, the tear in the lung being closed by a mattress suture if it was large or bleeding. The only lung wounds found to be bleeding were those held open by foreign bodies, and one in which the lung could not collapse because it was adherent to the parietal pleura; the bleeding in other wounds came from the chest wall, diaphragm, or abdominal cavity.

Having dealt with the lung the diaphragm was opened by enlarging the track of the missile with scissors, and the peritoneal cavity was explored. By observing the track of the foreign body through the chest wall and diaphragm a good idea of its direction could be visualized and its track through the peritoneal cavity followed. The most usual organ to be damaged was the spleen (9 cases), which was easily delivered into the wound and removed; in one case a partially divided splenic artery was bleeding furiously although the spleen was intact (*Case* 18). The rest of the upper abdomen was systematically examined and any lesions found were dealt with by the appropriate procedure; the stomach, transverse colon, spleen, body and tail of pancreas, first part of the duodenum, and the jejunum can all be explored and repaired by this route. In three cases only was the colon damaged—two wounds of the left chest and one of the right chest; their treatment is described under the case reports (*Cases* 7, 11, and 17).

All damage having been repaired, and the foreign body removed if it was found, the diaphragm was repaired with one layer of interrupted mattress sutures of 60 linen thread. The pleural cavity was then carefully cleansed with sucker and swab to remove all clots and the chest wall was closed by interrupted sutures while the lung was expanded with positive pressure. The wound being made airtight, the skin was then sutured and the dressing fixed with strapping. Any other wounds requiring treatment were then dealt with, after which the patient was cleaned and sent to the ward. The total operation time, from arrival to departure of the patient, varied between one and two hours.

On return to the ward penicillin therapy was continued, 15,000 units every three hours or 100,000 units in 24 hours by intramuscular drip. Continuous gastric suction, through a tube inserted by the anæsthetist in the theatre at the end of the operation, was maintained by a reversed drip bottle; morphine was administered every four hours and no food or fluid was allowed by mouth until peristalsis was again established and the gastric suction was clear.

Aspiration of the chest was performed next day and repeated every 48 hours if the radiograph or physical signs revealed an effusion. Several patients who had only clean-cut bullet wounds in the chest either did not require aspiration or needed it only once; 60,000 units of penicillin were introduced into the pleural cavity after each aspiration.

The last of the air was aspirated from the top of the pleural cavity by a needle inserted in the second intercostal space posteriorly and connected to a reversed drip bottle. This procedure was adopted in January, 1945, and was found to be a very satisfactory method of expanding the top of the lung.

Two patients with wounds of the right chest with liver damage are described (*Cases* 3, 12); two had anterior wounds (*Cases* 4, 13) and were explored by excising the wound of entry and continuing the incision downwards through the abdominal wall; two patients (*Cases* 15, 17) were explored from the abdomen, one (*Case* 15) because his extremely poor condition with obvious hæmorrhage warranted a rapid laparotomy to control his blood-loss, and the other (*Case* 17) because peritonitis had become well established during the 48 hours since he had been wounded. The only abdomino-thoracic wound (*Case* 10) was explored through the left loin, where there was a large ragged wound of entry involving the left kidney.

After operation the patients lay in the most comfortable position for 48 hours and then were placed sitting up and were encouraged to do breathing exercises and move their limbs. The intercostal incisions healed well and caused very little pain, patients with them being obviously more active and able to breathe better than their neighbours with abdominal incisions.

Immediate complications were few. Pericardial effusion occurred in *Case* 5, but quickly subsided; peritonitis in *Case* 7 was due to fæcal contamination; superficial sepsis complicated *Cases* 1 and 10, and failure in healing in *Case* 15.

Deaths were five in number: *Case* 2, a patient with four wounds in his chest, died from severe

hæmorrhage which caused much damage to his lungs; *Case* 13 from liver failure on the fourteenth post-operative day; *Case* 17 from peritonitis; *Case* 18 as the result of his enormous blood-loss; and one patient died on the table.

CASE REPORTS

Case 1.—Wounded 8 hours before operation. Entry wound through left 10th rib in mid-axillary line, piercing lung, diaphragm, spleen, and posterior wall of greater curvature of stomach. The spleen was removed and the stomach repaired; diaphragm and chest closed. Post-operative course was interrupted by superficial sepsis in the lower end of the wound. He still had a small effusion on evacuation to U.K.

Case 2.—Wounded 10 hours before operation. Entry wounds—four in left side of chest. Wounds involving 8th to 10th ribs excised and sucking wound of pleura enlarged. Lung very contused, two foreign bodies removed from rents in it. Hole through the diaphragm enlarged and a foreign body removed from the lumen of the jejunum, which was repaired. Diaphragm and chest wall closed.

Died on the fourth post-operative day; left lung was almost solid with hæmatoma.

Case 3.—Wounded 13 hours before operation. Entry wound through right 7th rib in anterior axillary line excised and a great quantity of blood evacuated from the pleural cavity. This blood was welling up through a hole in the diaphragm, which was enlarged; there was a large hole, taking the clenched fist, in the right lobe of the liver and passing towards the left lobe, in which a foreign body had been located by radiography. The cavity was packed with gauze roll, the end of the gauze being brought out to the surface outside the pleural cavity. The diaphragm was closed around the pack and sutured to the chest wall so that the main pleural cavity was sealed off from the pack. The foreign body was left in situ and is still there.

Penicillin was administered post-operatively by intramuscular drip.

The next day 300 c.c. of blood-stained fluid were aspirated from the pleural cavity.

Forty-eight hours after operation, under pentothal anæsthesia, the pack was withdrawn. No bleeding, no fluid in the chest.

He was evacuated on the tenth day, fairly well, with a slight bile-stained discharge from the wound.

Subsequently he arrived in the Queen Elizabeth Hospital, Birmingham (one month later), and a piece of necrotic rib and considerable amounts of necrotic liver were removed from an abscess under the original wound; a subhepatic abscess was also drained. He made a good recovery and now reports himself as very well and 2 st. heavier.

Case 4.—Wounded 6 hours before operation. Entry wound over 6th right costal cartilage excised and the incision extended downwards to open the abdominal cavity. The hole in the diaphragm was plugged by liver and there was very little soiling of the pleural cavity. The diaphragm was sutured and a hole right through the liver left alone as it was not bleeding much; a hole in the stomach was sutured and the wound closed.

Post-operative course was uneventful and the patient made a complete recovery.

Case 5.—Wounded 10 hours before operation. Entry wound through 9th left intercostal space was excised and the incision extended. There was a tear right across the dome of the diaphragm, a torn and bleeding spleen presenting in the wound. Splenectomy was performed and the foreign body was found in the pericardial cavity. After repair of the diaphragm the foreign body was removed, the pericardium sutured, and the chest wall closed.

A post-operative pericardial effusion gradually subsided, but the lung was difficult to expand fully. He was evacuated on the eleventh day and subsequently made a complete recovery.

Case 6.—Wounded 8 hours before operation. Entry wound in left chest excised and the hole in the diaphragm enlarged. The foreign body was found in the stomach, projecting through a hole in the greater curvature, which was repaired.

He was evacuated on the tenth day very fit.

Case 7.—Wounded 6 hours before operation. Entry wound in the left chest wall excised and extended. The pleural cavity was found to contain blood and fæces welling up through a hole in the diaphragm. The diaphragm was incised and a large tear found in the transverse colon. This was temporarily closed with a clamp while the other lesions were found and repaired. Holes in the jejunum and fourth part of the duodenum, just proximal to the duodenojejunal flexure, were repaired and the incision extended through the costal margin to allow exteriorization of the torn segment of colon. The abdominal part of the wound was then sutured, the diaphragm repaired, the pleural cavity cleaned, and the chest wall closed. A drain to the left hypochondrium was left in for 48 hours.

Post-operative intravenous sulphadiazine, 3 g. in alternate bottles of the intravenous drip, was administered in a dose of approximately 9 g. every 24 hours to a total of 21 g. Penicillin was given both intramuscularly and into the pleural cavity. His peritonitis cleared up and the chest gave very little trouble after the third day; he was evacuated in good condition, the colostomy working well, on the fourteenth day.

He subsequently had a superficial infection of the wound around the colostomy, but after ten months an enterotome was successfully applied and the colostomy closed. He is now well and at his business after a further short spell in the Army on Home Service.

Case 8.—Wounded about 8 hours before operation. Entry wound of right lower chest excised and a shattered rib resected. The hole in the diaphragm was enlarged and a ragged hole in the liver closed by mattress sutures, the missile had penetrated the liver to the kidney, but the hæmaturia stopped after 24 hours and was never profuse. The wound was closed as usual.

He made a good recovery and is now in the Army in the Middle East.

Case 9.—Wounded 3 hours before operation. Entry wound above the 10th rib excised and enlarged. A torn spleen was removed and two holes in the stomach repaired, the diaphragm and chest wall were repaired. He made a good recovery.

He also had a wound of the left thigh dividing both the artery and the vein which were ligated. The leg recovered a good circulation after 24 hours and the wound was secondarily sutured a week later. This man is still in the Army on Home Service.

Case 10.—Wounded 6 hours before operation. A large ragged entry wound of the left loin was excised and a disrupted kidney removed. The missile had then penetrated the spleen, which was removed, the stomach, which was repaired, the liver, and so through the diaphragm into the left lung. The liver was not bleeding and made an effective barrier against diaphragmatic hernia, so the patient was returned to bed and the chest treated by aspiration.

900 c.c. of blood were aspirated on the first occasion, 12 hours after operation, and 1000 c.c. of blood-stained

fluid 24 hours later. He was evacuated on the twelfth day after operation.

On return to U.K. he had some infection and superficial breakdown of his wound and was about to undergo secondary suture when he developed appendicitis. This was successfully treated by operation and his wound healed.

He is now very well and has put on 4 st. in weight, so that I hardly recognized him when I saw him recently. He is working.

Case 11.—Wounded 5 hours before operation. Entry wound of left chest excised and extended through the costal margin. Two small holes of the transverse colon were sutured and the foreign body removed from the transverse mesocolon, which required suture to stop free hæmorrhage. The damaged part of the colon was then pulled out as a diverticulum and attached to the abdominal wall outside the peritoneum (*Fig.* 217), the

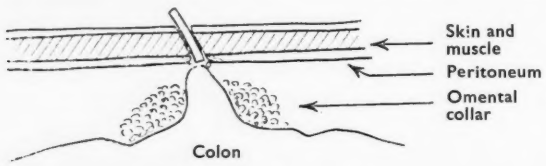

FIG. 217.—Diagram showing the method of extraperitoneal drainage after suture of a small hole in the colon.

diaphragm was repaired, the pleural cavity cleaned, and the wound closed, a small tube drain passing through the abdominal muscles to the colon diverticulum. The peritoneal cavity was not drained.

His chest was aspirated dry the next day, and the tube, which drained nothing, removed on the third day. He made an extremely rapid recovery and was evacuated on the eighth day. He was Category A again three months later, after two months on leave as Category D. He is still in the Army and playing rugby.

Case 12.—Wounded 11 hours before operation. A large sucking entry wound of the right chest was excised and free bleeding found to be coming from the liver. The liver was sutured and the diaphragm closed. Recovery uneventful and evacuated on the seventh day. He also had a through-and-through wound of the right arm with peripheral nerve involvement. He is now working in a garage and attending hospital for physical treatment of the right hand.

Case 13.—Wounded 13 hours before operation. Entry wound over the lower part of the sternum and right costal margin was excised and extended on to the abdominal wall. The right pleural cavity was widely open and a small tear in the left. The missile had passed through the liver at the portal fissure and was removed from a hole in the ileum. Two other pieces of metal were found in Morison's pouch. The liver was sutured and the diaphragm and pleura repaired.

The patient did very well for a week, then became jaundiced and died on the fourteenth day. Autopsy showed necrosis of a large part of the liver due to damage to the hepatic vessels.

Case 14.—Wounded 7 hours before operation. Entry wound through the left 10th rib excised and enlarged along the 10th intercostal space. The torn spleen was removed and the tail of the pancreas oversewn where it had been damaged. Some bleeding vessels in the omentum were ligated, the diaphragm and chest closed. He made an uninterrupted recovery.

Case 15.—Wounded 10 hours before operation. Entry wound was just below the left scapula running downwards to fracture the last four or five ribs. This patient was obviously bleeding freely inside the abdomen and chest and had not responded to transfusion; operation was considered urgent in spite of his very poor condition and low blood-pressure. Laparotomy through a left paramedian incision was performed and the abdomen found to be full of blood. The left kidney was torn in two and the diaphragm divided right across, allowing the stomach, which was very dilated, and a torn spleen, to go right up into the chest. A stomach tube was passed by the anæsthetist to release the air and fluid, the hernia was reduced, and the spleen removed. The patient improved now that bleeding was controlled, and the diaphragm was repaired from below and the abdominal wound closed. The patient was then turned on his side, the shattered ribs tidied up, and the blood rapidly sucked from the pleural cavity before it was closed.

Post-operatively he made slow but definite progress until the tenth day, when, on removing the abdominal stitches, the wound was found to be unhealed. He was re-sutured and given extra vitamin C. There was a residual blood-clot in the pleural cavity which prevented full expansion of the lung.

He arrived in U.K. by air on the thirteenth day after operation in fair condition. Two days later his stitches were again removed and again the abdomen fell open and was re-sutured.

He developed an empyema on the left side, which was drained, and he did very well. (Details from a 'follow-up card'.)

Case 16.—Wounded 7 hours before operation. Internal hæmorrhage increasing. Large sucking wound of chest wall excised and pleural cavity found to be full of blood. Diaphragm wound extended and a ruptured spleen removed; there was also a hole in the transverse colon and another in the stomach, both of which were bleeding freely. The viscera were repaired and the thread from the colon passed through the abdominal wall. The diaphragm was closed, but the patient died as the chest wall was sutured.

Case 17.—Wounded 48 hours before operation. Entry wound of right chest had penetrated the liver and the patient had established peritonitis. The abdomen was opened and nine holes in the small intestine were sutured, six more holes in a 5-in. length of ileum were resected, and end-to-end anastomosis was performed; a hole in the transverse colon was exteriorized and the peritoneum drained.

The patient died on the fifth day after operation.

Case 18.—Wounded 15 hours before operation. Very exsanguinated, but improved with massive transfusions. Entry wound of left chest excised and enlarged. The lung was adherent and since it could not collapse was continuing to bleed; two holes were sutured. A ruptured spleen was removed and the stomach, which had herniated into the chest, was returned to the abdomen. A very large amount of blood was evacuated from the chest and the wound repaired.

This patient died shortly after operation.

Case 19.—Wounded 4 hours before operation. Entry wound left chest excised and enlarged. A ruptured spleen was removed and a few bleeding points in the omentum tied. The diaphragm was repaired and the chest closed.

Post-operatively this patient had no pleural effusion to aspirate and made a rapid and uneventful recovery.

This man is still in the Army.

Case 20.—Time of wounding unknown, but he was an early case. Entry wound of left chest excised and enlarged. Ruptured spleen removed and a hole in the jejunum repaired. Diaphragm and chest wall closed.

He made a good recovery and was evacuated in very good condition on the twelfth day after operation.

SUMMARY AND CONCLUSIONS

1. A series of 20 operations for thoraco-abdominal wounds is described, with a record of the end-results as far as they are known.

2. Five patients died at, or soon after, operation—a mortality of 25 per cent. No patient died after leaving the Forward Area.

3. In agreement with other writers on the subject, I found the thoracic and diaphragmatic approach gave adequate exposure to the abdominal cavity, and was much less shocking and uncomfortable to the patient than an abdominal incision. The abdominal approach was used in one case with an entry wound in the loin and apparent damage to the kidney (*Case* 10); and in one case of increasing intra-abdominal hæmorrhage when rapid control of the bleeding was of vital importance (*Case* 15).

4. Wounds of the liver only may be treated conservatively unless hæmorrhage is great. The prognosis of all liver wounds is uncertain.

5. Careful cleansing of the pleural cavity should be an important step in the operation in order to minimize the risk of empyema and atelectasis. Introduction of penicillin into the pleural cavity after post-operative aspiration is advised.

6. Removal of air from the pleural cavity is accomplished by inflating the lung as the chest is closed and completed by continuous suction through a needle inserted through the 2nd intercostal space posteriorly when the patient is sitting up.

I am deeply indebted to Major K. R. Minto and to the Operating Room Assistants, Orderlies, and Drivers of my Field Surgical Unit for their skill and hard work in the theatre and wards; and to the Commanding Officers and all ranks of the Casualty Clearing Stations, Field Dressing Stations, and Field Transfusion Units, who gave us such excellent co-operation at all times.

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TRANSPLANTATION OF THE BICEPS TENDON AS A TREATMENT FOR RECURRENT DISLOCATION OF THE ELBOW

BY MAJOR P. P. REICHENHEIM, R.A.M.C.

RECURRENT dislocation of the elbow is very rare and there is no reference to it in the standard monographs on fractures and dislocations. There are, however, several cases reported in the American and German literature in the last half century. The case described in this paper is believed to be the first in this country.

CASE REPORT

Lance Corporal G., 25 years of age, had been a polisher in civilian life. There is no previous ill health.

When 13 years of age he sustained a dislocation of his left elbow following a fall on the left outstretched hand. The dislocation was reduced under gas and he was discharged from hospital an hour later with his arm in a sling. The elbow was swollen, painful, and stiff, but this gradually subsided and after four days he discarded the sling, as the elbow seemed all right again. There was then no pain, tenderness, nor limitation of movements.

Two years later he had a similar accident while playing football. This time a St. Johns' Ambulance man reduced the dislocation and put the arm in a sling, which was again discarded after four days. By this time the swelling of the elbow had subsided and movements were painless and full.

The third dislocation occurred when he was 19 years of age, again while playing football. While he waited for a doctor to arrive he flexed and extended his fingers. Suddenly he felt a click and "the joint went back on its own" ten minutes after the accident occurred. He carried on playing football and was able to move his elbow freely, but the next morning the joint was swollen and stiff and remained so for three or four days.

Between the ages of 19 and 22 he had two or three more accidents exactly similar to the first three, but on joining the army he was fit enough to be in medical category A.1. Since then he dislocated his elbow whenever he fell on his outstretched hand. On one occasion, however, it occurred while he was doing P.T. raising himself from the prone position on to his hands and knees. The accidents occurred with increasing frequency and ease, lately at the rate of about twice a month. During the last three years he dislocated his elbow about fifteen times. Last year he was admitted to a military hospital following one of his usual accidents. Here his arm was kept in a sling for three weeks; beyond that, he received no treatment.

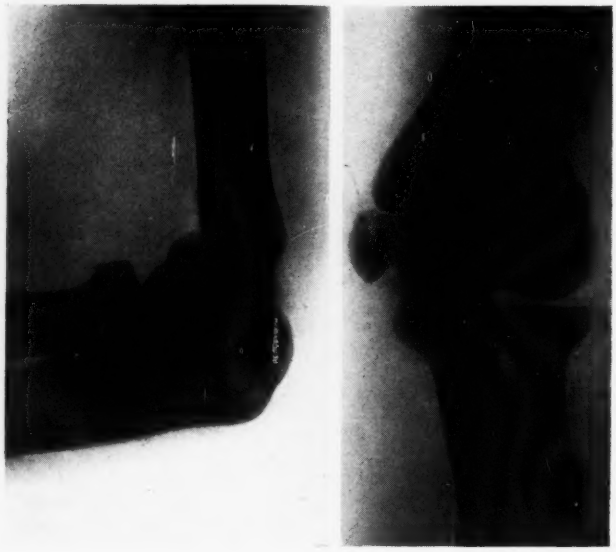
A typical accident was as follows: He fell on his left outstretched hand and experienced a sudden sharp pain in the back of the elbow. The elbow locked approximately at an angle of 140° and could not be flexed or extended. Finger, wrist, and shoulder movements, however, were free. He noticed that whenever he dislocated his elbow there was a marked depression anteriorly over the head of the radius. At first the dislocation was usually reduced by another person by longitudinal pull and quick pronation. Later on he was able to reduce it himself by quickly flexing and extending the fingers and pronating his wrist. He then felt a click in his elbow and reduction would be complete. Between these accidents there was no pain or tenderness and no limitation of movements, only a slight ache when he carried something heavy for a long time. Quick supination and pronation movements, however, e.g., turning on and off of a tap, gave him a pain and a feeling of insecurity in the joint.

No member of his family had ever had similar trouble with their joints and all his other joints were normal.

ON EXAMINATION (Aug. 21, 1946).—A healthy, well-built man with no obvious deformities. Both arms well developed and muscle power normal. The right elbow had a full and painless range of movements and no abnormality was demonstrable. The carrying angles were present and equal on both sides. In the left elbow movements were full and painless. Some fine silky crepitus was palpable on flexing the joint. There was slight tenderness over the head of the radius on full supination and at times a click was felt over the lateral aspect of the joint when the forearm was quickly pronated.

There was no abnormal mobility of the joint. No abnormal signs were demonstrable in the nervous or vascular systems.

X-ray Examination (Aug. 21).—The right elbow appeared normal with the exception of the medial epicondyle, which was separated from the rest of the bone and appeared to be united to the humerus by fibrous tissue only. The outlines of this fragment were rounded off and the whole epicondyle was surrounded by a clearly-defined layer of cortical bone. The epicondyle was displaced downwards, lying at the same level as the trochlea and capitellum (*Fig.* 218).



A B

FIG. 218.—Anteroposterior and lateral view of the right elbow, showing the ununited and displaced medial epicondyle.

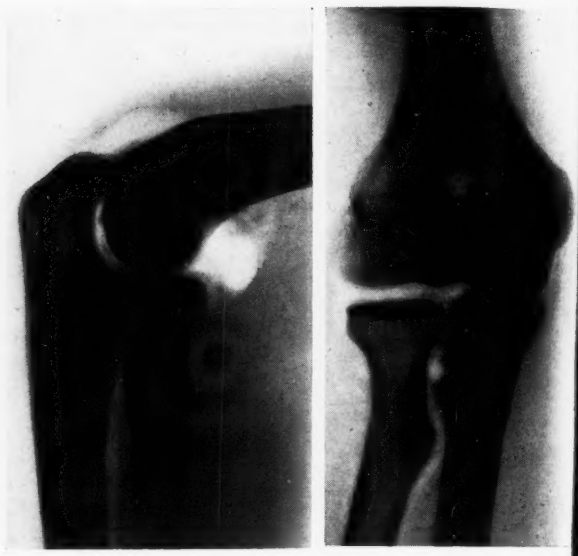
The left, recurrently dislocating elbow showed no abnormality in the anteroposterior view, but in the lateral view there was a striking shallowness of the trochlear fossa of the ulna, due to the absence of the tip of the coronoid process, the outlines of which appeared a little hazy. There was a shallow notch apparent on the articular surface of the trochlea.

To obtain further information air arthrography of the elbow-joint was performed on Sept. 1. The anteroposterior view showed no striking abnormality and it was obvious that the annular ligament was intact. The lateral view, however, revealed the joint capsule bulging out anteriorly and posteriorly to the humerus like a balloon (*Fig.* 219).

Under pentothal anæsthesia, by flexing the elbow to about 130° and pushing the ulna backwards, the ulna dislocated posteriorly with the greatest of ease. The dislocated joint was X-rayed again and then reduced easily by slight longitudinal pull of the forearm. The radiograph showed a posterior dislocation of the joint. It also revealed that there was one small irregular bony fragment near the tip of the coronoid process. The notch on the inferior surface of the trochlea was now very obvious and a small fragment of bone could be observed in the neighbourhood of the notch, an appearance suggestive of osteochondritis dissecans (*Fig.* 220).

TREATMENT.—In view of the above findings an operation was devised to stabilize the joint and prevent further re-dislocation.

Operation on Sept 9, under general anæsthesia. A pneumatic tourniquet was applied and the elbow-joint exposed by the approach devised by A. K. Henry. The incision started 2½ in. above the level of the elbow-joint along the lateral border of the biceps tendon, bending medially opposite the bend of the elbow and running along the middle of the forearm for another 2½ in. The lateral branch of the medial cubital vein was divided and the vein retracted medially. The brachioradialis was retracted laterally and the lateral border of the biceps tendon was now followed downwards. The only obstruction encountered was the leash of vessels springing from the radial recurrent artery. After dividing this vessel it was easy to clear the biceps tendon down to its insertion and to displace the neurovascular bundle, comprising



A B

FIG. 219.—Air arthrography of left elbow, anteroposterior and lateral views. In the anteroposterior view the intact annular ligament of the radius can be observed. The lateral view shows the absence of the tip of the coronoid process and the notch on the inferior surface of the trochlea.

the median nerve and radial artery and veins, medially. In the floor of the wound the lower fibres of the brachialis muscle were now clearly exposed. The muscle was split longitudinally for 2 in. from its insertion upwards. The anterior surface of the elbow-joint now came into view and the blunt coronoid process of the ulna, together with the small bony fragment connected to it loosely by fibrous tissue, was apparent. The anterior capsule of the elbow-joint was extremely thin and almost translucent. The tendon of the biceps was cut near its insertion and layed into the groove made by the longitudinal splitting of the brachialis, thus lying in front of the lower end of the humerus and the joint capsule. The elbow was flexed to 130°, the biceps put on tension, and the tendon sutured to the tough periosteum covering the lower and anterior aspect of the coronoid process with two silver wire sutures (*Fig.* 221). The split in the brachialis was closed in front of the biceps tendon by interrupted sutures and thereby a muscular tunnel was formed underneath which the biceps tendon ran to its new insertion. After suturing the skin the elbow was fixed in 130° flexion by a plaster-of-Paris backsplint.

AFTER-TREATMENT.—The arm was kept on a plaster backsplint for three weeks. Meanwhile wrist and shoulder-joint were freely exercised. On Sept. 29 the splint was taken off and gradual exercises begun, but between exercises the arm was still worn in a sling for a further five days. Exercises were continued, and by Oct. 10 pronation, supination, and flexion were full, but extension limited to 140°. It was interesting to observe

that the power of supination seemed to be little diminished. By Oct. 30 extension had increased to 170° and the strength of the arm was very good indeed and only slightly less than in the right arm. In the meantime the patient had played several games of football and volleyball without experiencing the slightest inconvenience, although he stated that he was careful not to fall on his left hand. He was now able to supinate and pronate his forearm quickly without any pain and any sense of insecurity.

DISCUSSION

Bloch was apparently the first to describe recurrent dislocation of the elbow in 1900. Lexer and Peritz (1924) described two more cases. The dislocation was a posterior one in all reported instances

FIG. 220.—Air arthrography of the dislocated left elbow. The bony fragment near the tip of the coronoid process is now visible.

with the exception of Rehns's (1924) patient, who had a recurrent forward dislocation of the elbow. Sommer (1928) first tried to classify the different aetiological factors leading to this condition. He divided them into those where there were no apparent bony changes, but the extreme laxity of the joint capsule allowed recurrent backward displacement of the ulna on the humerus (as in the patients of Knoflach, Grossman, and Sorrel), and dislocations occuring in joints with changes in the bony structures. Bony changes he subdivided into :—

1. Congenital malformation of the ulna, of which Milch's case, which is to be discussed in more detail later on, was an excellent example.

2. Bony changes caused by trauma. This appeared to be the aetiological factor in the recurrent dislocation described in this paper, although it was also associated with great laxity of the joint capsule.

3. Bony changes on a possible basis of osteochondritis dissecans as postulated by Sommer in his case.

Knoflach in 1935 described an operation in an attempt to cure the disease. His patient was a boy of 14, who during the previous four years dislocated his elbow nine times by falling on the outstretched hand. Great laxity of the joint was found on examination, but X-ray pictures showed no bony changes. To stabilize the joint he performed a capsulotomy by plicating the anterior capsule of the elbow and further strengthened it by suturing 1-in. broad strips of fascia lata crosswise in front of the joint, anchoring the strips of the periosteum of humerus, ulna, and radius respectively. After immobilizing the joint in plaster for four weeks and then carefully exercising the arm the boy made uninterrupted recovery, and at the time of writing the paper he had not redislocated his elbow during the ten months following the operation.

Milch in 1936 was the first American surgeon to describe a case of recurrent dislocation of the elbow. He was not aware of the work of the earlier German workers and considered his case the first one with the exception of one reported by Sorrel in

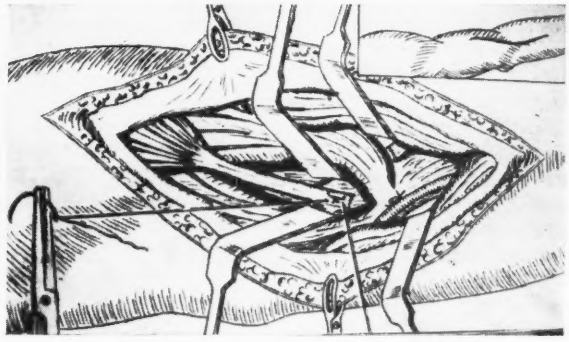


FIG. 221.—Sketch of biceps tendon transplantation. The brachioradialis is retracted to show the distal stump of the severed biceps tendon, the retracted pronator teres makes the medially displaced radial artery and median nerve visible. The biceps tendon is fixed to the anterior aspect of the coronoid process. Inset shows the incision.

France. His patient, a boy of 17, had a congenital shallow trochlear notch of both ulnas due to partial absence of the coronoid process. He dislocated the right elbow eight times and the left four times. On examination the carrying angle of both arms was obliterated. Milch used a boomerang-shaped bone-graft from the tibia, which he impacted into a notch cut in the stump of the coronoid process, thereby achieving a bony block to prevent further redislocation. The boy made an uninterrupted recovery, regaining full movements of the joint with the exception of a slight limitation of extension. Milch mentions an alternative possibility of treating the lesion by juxta-articular osteotomy of the ulna to increase the depth of the trochear notch.

In 1943 Grossman described another case. His patient was the only female in the series, a girl aged 15, who dislocated her elbow five times. The elbow-joint was hypermobile. Flexion was in excess of normal and she could extend the elbow to an angle of 195°. There were no bony changes visible on X-raying the joint. He performed Milch's operation with the simplification of using a rectangular bone-graft instead of a boomerang-shaped graft. The result, however, was not entirely satisfactory, as although no redislocation occurred the patient could only flex her elbow up to an angle of 135° one year after operation.

Apparently Dzanelidze (1937) described a case of habitual dislocation of the elbow, but the paper is unobtainable.

In the case described in this paper the original injury was most likely a posterior dislocation of the elbow with fracture of the coronoid process. This is not an uncommon injury and in Wilson's large series occurred seven times in 350 cases of fractures and dislocations near the elbow-joint. After the patient's first accident the arm was only kept in a sling for four days. It seems possible that the fragmented tip of the coronoid process united therefore by fibrous tissue only and so permitted further dislocations because of the shallowness of the trochlear notch. The laxity of the capsule appeared to be a secondary development because of the frequent stretching during dislocations. The appearance of the inferior surface of the humerus suggested that recurrent impingement of the coronoid process during dislocations produced changes in the inferior part of the trochlea resembling ostochondritis dissecans.

When the patient was first seen the articles in the literature were not available. Three methods of treatment were considered—namely, capsulotomy, bone-grafting to increase the size of the coronoid process, and transplantation of the biceps tendon into the ulna. Capsulotomy has generally been discarded as a most unsatisfactory treatment for any joint condition. The employment of a bone-graft seemed needlessly complicated and it was feared that limitation of flexion might result. The transplantation of the biceps tendon appeared to be the method of choice as the stability of a joint depends on the strength of the muscles acting upon it. Furthermore, as the causative injury in this patient was always a fall on the outstretched hand, it was thought that the automatically contracting biceps would, by its pull, prevent any displacement of the ulna during such an accident. To give added stability the biceps tendon was transplanted in front of the elbow-joint behind the brachialis muscle. The operation had the advantage of simplicity and was nearly completely bloodless thanks to A. K. Henry's excellent approach.

Although it is impossible to say with certainty that the patient will be free of any recurrence, so far there has been no further dislocation and the man is back on full duty with the army.

SUMMARY

A case of recurrent dislocation of the lett elbow is reported. The possible aetiology of the condition is discussed. Previous cases and their treatment are noted and a new operation for treating the lesion is described.

I am most grateful to Lt.-Col. J. M. Small, R.A.M.C., on whose original suggestion the operation was based, for his help and advice both with the treatment of the case and the preparation of this paper.

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NOTE ON CRANIAL AUTOPLASTY

BY H. P. PICKERILL, C.B.E.
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To the plastic surgery minded surgeon always seeking new and more suitable donor areas, it would seem that the inner plate of the ilium was provided for his special benefit in restoring to normal any loss of the cranial vault which a human being is likely to survive, so perfectly is it adapted to this purpose.

Some sixteen years ago the writer described such a method, but it does not seem to have met with that general acceptance which its intrinsic merits would seem to deserve.

Woolf and Walker (1945), in an extensive review on cranioplasty, state that "Mauclaire in 1914 repaired a cranial defect with a graft from the crest of the ileum, Phemister (personal communication) used the outer table and Pickerill (1931) the inner table". These reviewers also state: "The ideal repair of a cranial defect is the regeneration of the bony calvaria—although attempts have been made to stimulate osteogenesis in soft tissues over a bony defect, satisfactory clinical results have not yet been obtained. Autogenous bone-grafting may serve as a skeleton for the regeneration of new bone. In the final analysis, however, the success of this technique depends upon the fate of the transplanted bone. If the graft is absorbed and replaced by fibrous tissue, it cannot fulfil its purpose adequately; but if it remains viable or is replaced by living bone it is pre-eminently satisfactory."

The allusion in the above quotation is to an article by the present writer in 1931 on the use of the inner plate of the ilium and the restoration of cranial defects; a case so treated was subsequently shown at the meeting of the Australian College of Surgeons in Auckland in 1936. Woolf and Walker further state "the fate of a cranial bone-graft has not yet been determined". The follow-up of these cases after a number of years is difficult; so many patients in this part of the world change their abode frequently and cannot be traced. It was whilst considering how this question could be answered that I was more than pleased to receive visits from three patients on whom I had operated many years previously. The details

of these cases will be discussed further on, but none of the patients had any complaint and had merely called to report that all was well—would that more patients would do the same sort of thing.

What are the desiderata for closing a cranial defect ? I trust that neurosurgeons will forgive these suggestions, but it seems to me that this is a

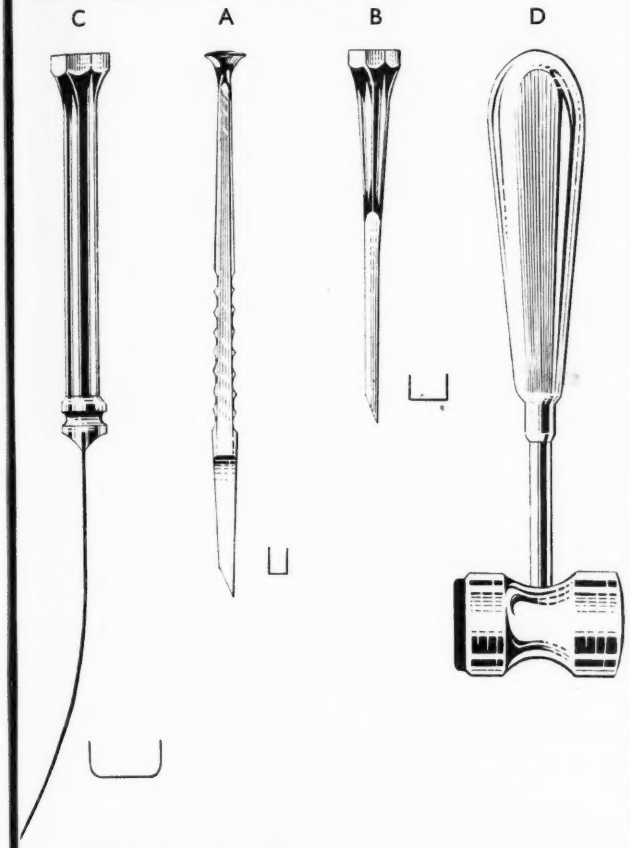

FIG. 222.—Instruments recommended for grafting the skull from the ilium. (*Four-sevenths scale.*)

A, B, Chisels used for bevelling the skull margins and also for outlining and cutting round the iliac graft.

C, Curved and slightly flexible osteotome for cutting through the cancellous bone of the ilium.

D, 6-oz. mallet. If a heavier mallet is used accidents may happen.

To test the efficiency of the curved osteotome place the cutting edge on a piece of cardboard on a table, and holding the handle nearly upright tap smartly with the mallet. The cutting edge of the osteotome should slide along smoothly parallel to the table top.

matter in which the experience and technique of plastic surgery may be of assistance to them.

I would enumerate the desiderata thus :—

1. No scar tissue to be left on the surface of the dura or brain.

2. A perfectly smooth surface to be next the dura, with no angles, sharp edges, or corners to serve as possible irritants.

3. The curvature of the material should be that of the surrounding calvarium.

4. The material should be non-conducting, thick, living, and preferably the same tissue as the rest of the skull, i.e., bone.

In other words, the plastic surgeon's ideal—the restoration of the normal—should be aimed at.

Other bones such as rib and tibia fulfil some of these desiderata, but are either flat, not wide enough, not of the correct curvature, or may present a rough cancellous surface to the dura. Bone-chips have been used for this purpose, but this destroys one of the most important desiderata, namely, a perfectly smooth surface next the dura. I cannot imagine anything more likely to cause adhesions and therefore irritation and possibly convulsions. Vitallium, if cast for each case to fit accurately, fulfils several desiderata, but it is certainly not non-conducting, and if it should be in the least degree too big or out of shape it is so hard that it can neither be cut, nor filed, nor bent.

The use of tantalum it would seem has similar defects—it leaves either angles and sharp corners around the margins or dead spaces ; it can be cut and adapted to any case in one operation, but is certainly a conductor of heat, cold, and electricity.

Acrylic has nearly all the desiderata if it is made to fit accurately from an impression of the defect in each case. Its only drawback is that it must be thick to be strong, and because it undergoes some change with age we do not yet know its limitations. It is well tolerated by the tissues, but it is not living tissue, and two operations are required.

In considering the relative values of vital versus non-vital restoration, the effect on the psychology of the patient has to be considered. Mentally, physically, and psychologically, the man with ' a plate in his head ' is a very different man from one who is convinced that his skull is now whole and ' as sound as it ever was ', which he often demonstrates by tapping hard over the grafted area.

The apparent disadvantages of using living iliac bone to restore a defect are the supposed difficulties of the operation, " the necessity of having two operating teams " and "the liability to fracture the ilium ". It may therefore be of advantage to describe in detail the technique which I have found to be both simple and effective and which disposes entirely of the above imaginary or unnecessary complications.

From a long experience of the ilium as a donor substance for grafting the mandible I am convinced that—providing : (*a*) the fit is mechanically accurate, (*b*) there are no dead spaces, not even minute ones, (*c*) the cancellous bone is well exposed for early vascularization, and (*d*) the aseptic technique is sound—iliac bone lives, and does not absorb and become replaced by either fibrous tissue or new bone, as more dense bone like tibia may do and often does.

The great advantage of iliac bone is that there is available a layer of cancellous bone plus a thin but strong layer of compact bone, and I think it is the ready vascularization of the cancellous bone which enables the compact bone to live without absorption.

TECHNIQUE OF OPERATION

1. The area of loss having been exposed by a suitable flap considerably larger than the defect, all scar tissue is removed.

2. All eburnated bone margins (*Fig.* 223 A) are removed until bleeding points are freely visible.

3. The bone margins are then bevelled to an angle of 45° (*Fig.* 223 B) by rongeurs and fine small chisel (*Fig.* 222 A, B) used parallel to the bone margin.

4. A pattern of the area is now cut in thick sheet pewter (*Fig.* 223 B) which should conform fairly accurately to the outer bevelled margin.

5. The inner plate of the ilium is exposed by an incision along its crest and the periostium and iliacus muscle stripped and held back with a broad retractor by an assistant.

6. Having found the most suitably curved portion of the exposed bone, the pewter pattern is placed on it and held there with the two points of a pair of strong dividers, and with a sharp trocar point a deep scratch is made into the bone all round the margin of the pewter.

7. With a short (4–5 in.) sharp osteotome and a small mallet (*Fig.* 222 C, D), the bone is cut along the previously made scratch. This is the only really difficult part of the operation—namely, to be able to make a running cut with a chisel or osteotome and to follow a definite curved line. (Previous practice on wood, bone, or metal is desirable.)

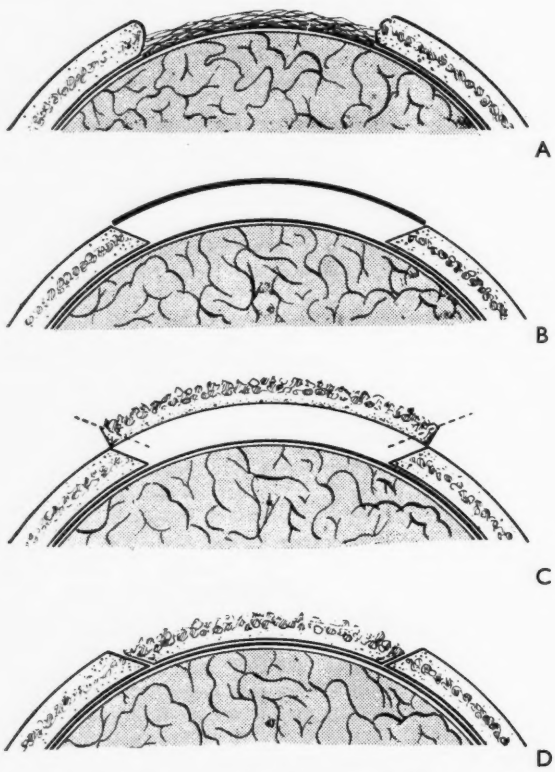

FIG. 223.—Diagrams to show the principal steps in filing the iliac graft to the skull.
A, Showing irregular and eburnated margins of defect and scar tissue.
B, Margins of defect bevelled to 45° and scar tissue removed. Thick pewter pattern cut to fit the top margin of the bevel;
C, Graft from inner surface of ilium consisting of compact smooth bone downwards and cancellous bone upwards, removed and placed over the defect;
D, Margins of the iliac graft bevelled by filing to fit accurately into defect—re-apposition of the scalp-flap is the only fixation necessary.

8. With a thin curved osteotome inserted in the margins of the now island of bone, the underlying cancellous bone is cut through. This requires care and to be done very gently or the proposed graft will be fractured. I imagine that the accidents which have been reported, such as serious fracture of the pelvis, have resulted from using unsuitable instruments and too much force. Accuracy and gentleness must be the keynotes. Unable at first to get a suitable instrument, I adapted a metal-handled table knife to the purpose and this really served the purpose excellently. It was simply narrowed, sharpened at the end and the blade suitably curved. The assistant must be on the look-out for undue bending of the graft and must speak up quickly to avoid disaster; by this means I have never, fortunately, fractured a graft (or the pelvis!). It is a little easier to remove the graft if one margin can be made to correspond with the crest of the ilium, thus facilitating the insertion of the curved osteotome. This position, however, is not always possible without sacrificing suitability of curvature of the graft.

9. The graft being safely secured it is removed to a prepared table for shaping (*Fig.* 223 C). It has to be kept well in mind that the smooth compact or downwards surface must be smaller than the cancellous surface. This is effected by small rongeurs and small coarse files such as are used for filing vulcanite, until a bevel of 45° is provided all round. It is then repeatedly tried in place on the skull and filed where necessary until an accurate fit all round is obtained, when it will be found that the graft sits in place and it feels obvious that when it is covered by scalp and bandage there will be no tendency to, or possibility of, movement (*Fig.* 223, D). At first I drilled holes in the graft and cranium and used chromic gut sutures, but further experience has shown that this is not necessary—provided the fit is accurate—and if it is not so, the graft will probably not live.

10. The scalp flap is returned, and I usually insert two fine rubber-dam drains for 24 hours at the most dependent points, since it is most desirable that no blood whatever should collect between the cancellous upper surface and the scalp, from whence will come its early nourishment (*Fig.* 223, D). A firm crêpe bandage completes the operation.

11. The closure of the iliac area requires a little comment. Immediately the graft is removed from its bed the latter is packed firmly with one or two swabs wrung out in hot saline, and the wound edges brought together temporarily with a wide mattress suture.

On completion of the head operation the surgeon himself should carefully inspect the donor bed for bleeding points; I have used bone-chips, Horsley's wax, and muscle for these and the latter I find effective. There is undoubtedly a tendency for hæmatoma formation and for this reason I have always drained the area for several days, allowing no collection of blood to take place. This may mean very careful and frequent dressings, but apart from a little consequent delay in healing I have experienced no trouble nor has any patient complained of any disability.

I have not done this operation since fibrin foam and thrombin have been available to me, but with the use of these agents I should not anticipate any trouble whatever from post-operative bleeding from the ilium.

CASE REPORTS

Late histories of the cases previously mentioned:—

Case 1.—A boy, aged 14, was attacked by a lunatic with a tomahawk; he lost nearly the whole of the right

half of the frontal bone and a considerable hernia cerebri developed. Seventeen years ago, in 1930, I did an internal plate of ilium graft exactly as above described, which went very smoothly. Now in 1947 he is married, has three children, and is running a large dairy farm—and that means physical fitness if anything does. When I saw him he was smiling, happy, and still grateful, he tapped his graft with his fingers and said he was " quite sound in the head "! On palpation the graft could be identified with certainty by the slight elevations at the margins and the original unevenness of the cancellous upper surface could be identified. There was to me no question whatever but that it was the original living graft in situ and that no absorption had taken place; the only difference being that the scalp was adherent in this area and not mobile as elsewhere, and this attachment, of course, is necessary for the survival of the graft.

Case 2.—A soldier in World War I suffered a shrapnel wound of the forehead with considerable loss of bone. He had spent the subsequent fourteen years doing nothing, convinced he was " no good ". Much money had been spent on him by the State and his friends in an endeavour to improve his mental condition without any success. Then, fifteen years ago, he came under my care and I successfully repaired the loss of bone with an internal iliac graft. From then be became a different man, the swing at first was a little too extreme, but he settled down well. When World War II broke out he enlisted in the Air Force, became a sergeant, and served for three and a half years, but he said, " I never told them that I once had a hole in my head "—whether " they " knew or not I cannot say. The graft is solid and in good position, and he says he has no complaints. He is married and fruit farming successfully.

Case 3.—Soldier of World War II suffered a shrapnel wound of the forehead with complete loss of the supra-orbital ridge and partial loss of the roof of the orbit. When I saw him in 1942 the wound was well healed, but there was a large pulsating swelling all along the left supra-orbital region and the left eye was missing. He was sent to me because he had headaches and " moped ". His father said he would do nothing but mope by the fireside all day, and would not associate with his previous friends nor do anything on the farm. He was willing to be operated on but quite evidently did not think it would do any good. Restoration in this case was carried out by utilizing the crest of the ilium to form the supra-orbital ridge and the attached inner plate to form the roof of the orbit, which demonstrated very well how adaptable this donor area is. When he came to see me, four years later, he was smiling and well dressed and said he had come to town to buy an engagement ring ! He now had a farm of his own, he said, and was working hard and milking cows. " Do you push your head into the cow's flank like others do when milking ", I asked. " Yes ", he said, " just the same, I'm not afraid at all ". On examination the graft was in good position, quite firm, there was no tenderness and no headaches. He admitted to some " curious feelings " in the area sometimes, but could not further describe them. The psychological transformation was complete and was largely so because " the hole had been filled with his own bone which had grown there ".

Case 4.—This, though a tibial graft, may be of interest since it was done in 1919 at Sidcup in the presence of no less a critic of bone surgery than Sir Arbuthnot Lane, who watched me (I felt) intently for over an hour, and at the end, removing his 8-fold mask, simply said to my great gratification, " Well done ". The patient was an infantry officer of World War I, with a wound of the right parietal region with loss of bone. Mental depression and headaches were a marked feature. Restoration was by similar technique but using the anterior surface of the tibia, smooth surface downwards. When I saw him eighteen years later, the graft was in good position and firm. He was a busy and successful professional man, played a good game of golf, and sailed his own yacht without any fear. Tibial graft was used because it had not then occurred to me to use ilium, and the width of the loss just equalled the width of his tibia, and was just over two inches long. The comparatively flat temporoparietal region of the skull is the only one for which a tibial graft may be considered suitable, but I believe the risk of a non-take is much greater than with ilium, because of its greater density. When the loss of bone is circular and from a curved surface of the skull, tibia is not a suitable donor ares. The external plate of the ilium would be quite suitable for some grafts, but it is much more difficult of access—the massive glutei muscles and the great trochanter prevent anything but a small area of bone being removed successfully.

These follow-up histories over a long period help satisfactorily to answer the point raised by Woolf and Walker that we should know more about the ultimate fate of these grafts before using them. In my experience there is only one reason (given a dead accurate fit) which will cause an iliac bone-graft to absorb and that is infection; but now with penicillin, even that is apparently no bar. Two teams, as suggested, are not necessary—one surgeon in my opinion should be responsible for both areas. I have never had more than one assistant. The operation takes from one to one and a half hours. The fact that each of these patients has been doing very active work continuously since his operation, shows that no disability resulted from the iliac donor bed.

There is only one drawback and that only from a record point of view—no satisfactory radiograph can be obtained afterwards to demonstrate the presence of the graft, since there is only one table of compact bone whereas the rest of the skull has two, and the rays before passing through the graft have of necessity passed through two compact tables and the third thinner one makes no difference.* It might, however, be of considerable interest to compare a series of E.E.G.'s taken after restorations by metals, plastics, and iliac bone-grafts in different patients; in this way physiological if not anatomical benefits or disadvantages may be demonstrable. There is no doubt whatever that surgically, anatomically, and psychologically the patient's own tissues make the best restoration, and, as I have previously pointed out, the more " like to like " the operation can be made the more likely it is to be successful.

At the conclusion of an operation such as described one has a feeling of considerable satisfaction that the best possible thing has been done for the patient, that it will function and endure, that as nearly as possible the surgical ideal has been attained of the restoration of the normal.

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* Two radiologists in Sydney, one in Auckland, and two in Wellington all concur that it is not possible to demonstrate the graft.

In Memoriam

PROFESSOR ELLIOTT CARR CUTLER

Boston, Mass., U.S.A.

THE death of Elliott Cutler, Moseley Professor of Surgery, Harvard University, and Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston, will occasion deep sorrow in the hearts of his many friends in the United Kingdom. Perhaps no surgeon of the United States ever yearned or strove more earnestly to forge lasting bonds of friendship, not only between the surgeons, but between the peoples of the great English-speaking countries on either side of the North Atlantic, and to this end he directed both written and spoken word.

ELLIOTT CARR CUTLER
1887—1947

His ancestry was one of which he was justly proud; his forbears had crossed the seas from East Anglia in the days of the *Mayflower*; he came of a family deeply respected along the whole eastern seaboard of the U.S.A., and the calibre of the modern Cutler stock may be gauged by the fact that in the recent war two of the Cutler brothers attained the rank of Brigadier-General, while a third became a Rear-Admiral in the United States Navy.

Elliott's culture bespoke the city of his school-days and the University of his training, to which he was destined to return in mid-life as Moseley Professor of Surgery. The early post-graduate years were passed in many places, in clinics in his own country and on the European continent: he worked under the great Halsted and Cushing, Czerny of Heidelberg, and Perthes of Tübingen. The first world war brought him in close contact with British surgeons, and friendships were forged with English

and with Scots which lasted as long as life endured.

The professorial period of his career was spent in Western Reserve University, Cleveland, Ohio, and afterwards at the Peter Bent Brigham Hospital, Boston. He did pioneer work in the surgery of the thyroid and the heart.

His full and eager life left little time for the writing of books; his reputation will not rest on that *insanabile scribendi cacoethes* which so often advertises a name but not the worth or character of the writer: for character is rarer than genius; it is the most enviable of all the gifts.

His well-stocked library and his fastidious choice of books proclaimed the discerning bibliophile and at the same time gave him a mastery of words and of clear and delightful expression.

> "His ready speech flowed fair and free
> In praise of greatest courtesy."

He was fluent in many tongues.

In Elliott Cutler no more happy choice could have been made of a chief consulting surgeon for an army that was to be transported to Britain, to train alongside an ally in the land of an ally, and to fight alongside that ally on the battlefields of North-west Europe.

The long period of training of troops and preparation in Britain for the invasion of the Continent happily brought Elliott Cutler into the closest contact with many British surgeons, and he was a frequent and always welcome visitor at the Royal College of Surgeons of England and the Royal Society of Medicine. Both bodies made him an Honorary Fellow before the end of the war, as did the Royal College of Surgeons of Edinburgh. He was placed on the Editorial Committee of the BRITISH JOURNAL OF SURGERY.

He had many surgical honours conferred on him by his own profession in the U.S.A., notably the Bigelow Medal, a distinction conferred on the most eminent in the world of surgery, such as Alan Whipple, Grey Turner, and others. Perhaps he was most proud to have been awarded, by his own country, the Legion of Merit a second time, not long before his death.

With Sir Henry Tidy and L. R. Broster he instituted the successful monthly Inter-Allied Conferences which were held within the precincts of the Royal Society of Medicine, where medical and surgical problems of Service interest were discussed under security. To these meetings came representatives of all the Allies, and none will readily forget the E.T.O.U.S.A. Medical Headquarter Group—Paul Hawley, Elliott Cutler, Kimbrough, Morton, Kneeland, "Bill" Middleton, and others. Elliott's wonderful tact and diplomacy at these Inter-Allied Conferences will long be remembered by those privileged to attend. While loyal to the opinions expressed by his American colleagues, he was not forgetful that in war experience counts, and that he and his officers had much to learn from us in Britain.

It was said of Homer that he "praised almost everything, and that he passed over nothing without somehow honouring and glorifying it". This was true of Elliott's references to the work and words of the medical officers of all the Allied Armies.

The tall, erect, soldierly figure, elegant and well-groomed; the silver hair; the shrewd, candid, but kindly eyes; the charming smile; the attractive drawl, punctuated by sudden bursts of swift-flowing words from his lips, which almost compelled appreciative imitation, made this great surgeon a seeming paladin, while these natural gifts and his intense desire to further the Anglo-American entente made him perhaps the finest ambassador in surgery the world has known.

With his large heart he might have exclaimed in the words of the great Scottish novelist when death seemed to hover near, "For myself I am unconscious of ever having done any man an injury or omitting any fair opportunity of doing any man a benefit". His life and professional position were directed not *pour chauffer la gloire* for himself, but to secure a just appreciation of the work and worth of the young surgeons whom he had trained, who adored him, who accompanied him overseas in their numbers during the recent war, and who are now carrying on the 'Cutler tradition' in numerous surgical posts across the Atlantic.

He died of a malady such that he was well aware for over two years of the end which inevitably awaited him. His supreme courage evoked the admiration of all associated with him in the work of his clinic and of visitors and friends who were permitted to know the stark truth. Throughout this period "deliberate valour breathed". The oar was, perhaps, pulled with slightly less vigour, but the pace of the craft never slackened; he "reefed no sail".

Despite his illness he retained supreme interest in the work of the surgical department of his hospital, and in the organization of the arrangements for the treatment of the veterans of the war, travelling thousands of miles in his capacity as Chief Consultant,

> "Who not content that former worth stand
> fast
> Looks forward persevering to the last,
> From well to better daily self-surpassed."

We are told, if you pass any country burial ground in Sweden, you may to this day see bareheaded peasants bending over a grave, and may catch the muttered words of their liturgy:—

> "*Integer vitæ scelerisque purus.*"

Such might be the epitaph of this 'Happy Warrior'.

SHORT NOTES OF RARE OR OBSCURE CASES

A CASE OF LIPOMATOSIS OF THE TONGUE

By ANDREW M. DESMOND
ST. JAMES HOSPITAL, BALHAM

ALTHOUGH several cases of lipomata of the tongue have been recorded in the literature, it is undoubtedly a rare condition. They may occur at any age. Chipault (1890) reported one in a child aged eighteen months which he considered congenital; Sewell, quoted by Duncan Fitzwilliams (1927), removed one from a man aged 86 years.

Most commonly they occur on the lateral borders, usually in the anterior two-thirds, but they may also appear beneath the tongue and involve the floor of the mouth or on the posterior third and project into the pharynx. They are usually submucous, in which case the diagnosis is obvious, but they may be intramuscular and only on removal or when they become large enough to reach the surface, does the diagnosis become manifest. They may be pedunculated or sessile, single or multiple. They are soft, circumscribed, and present a yellowish tinge. They are usually brought to the notice of the clinician only when large enough to interfere with the functions of the tongue, mouth, or pharynx.

The differential diagnosis has to be made from ranulæ, sarcomata, abscess, or gummata. Dufourmentel, quoted by Fitzwilliams, recorded one which had grown into a dental gap and was thought to be a cyst.

The treatment is simple enucleation, which can be performed easily under local anæsthesia. Hæmorrhage is usually minimal and readily controlled by suture.

Diffuse lipomatosis is extremely rare and I could find only one case recorded in the literature. This was described by Bond (1898) and was associated with diffuse lipoma of the parotid region which had extended inwards and spread along the side of the tongue beneath the mucous membrane.

The following case of true primary lipomatosis of the tongue is therefore recorded as possibly unique.

CASE REPORT

HISTORY.—F. S., aged 67, a mentally defective male, was admitted to St. James Hospital, Balham, from a mental hospital, complaining of the constant protrusion of his tongue.

He had been in mental institutions all his life. He was a mild diabetic, but although he had an hypoglycæmic attack shortly after admission, he was well controlled by a diet and 15 units of soluble insulin daily. A history was given that a lump was removed from his tongue previously, but details of this were unobtainable.

ON EXAMINATION.—He was somewhat wasted and obviously mentally deficient. His tongue constantly protruded from his mouth and his speech was almost incomprehensible. He had considerable difficulty in masticating his food as the protrusion prevented mandibular occlusion.

The tongue (*Fig.* 224) was large and presented a pinkish yellow tumour 2·0 cm. diameter on the left side of the tip. Along the lateral borders were multiple small yellow tumours. All were soft but not palpably lobulated and were confined to the anterior two-thirds. The central part of the tongue had a faint purplish hue, but appeared otherwise normal. No tumours were noted in the posterior third.

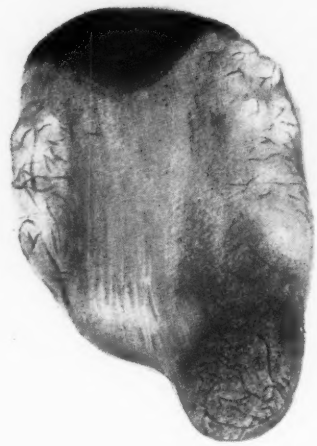

FIG. 224.—Showing appearance of the tongue before operation.

No lipomata were discovered elsewhere in the body and general physical examination was normal.

TREATMENT.—One of the tumours on the left side was removed under local anæsthesia (1 per cent procaine). It was shelled out with great ease and very little bleeding. Sections showed a typical lipoma. One week later the large tumour at the tip was similarly removed and also proved to be a lipoma 2·0 cm. diameter. In order to restore satisfactorily the shape of the tongue, a small wedge resection of the bed of this lipoma was performed and it was then noted that the muscle tissue was replaced by a diffuse lipomatosis and consisted almost entirely of masses of seedling lipomata. The wound healed rapidly and the tongue no longer protruded from the mouth. Diction was considerably improved and good mastication of food was once more possible.

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ORBITAL HYDATID

By DOUGLAS MILLER and J. L. DOWLING, Sydney

CASE REPORT

R. L., a strong healthy girl aged 4½ years, a country dweller, had a history of a gradually increasing protrusion of the left eye for four months. There was an associated disturbance of vision.

On Examination.—There was marked unilateral non-pulsating exophthalmos of the left eye, which was displaced downward and outward. There was a paresis of the superior rectus muscle. The right optic disc showed a high-grade papillœdema. The visual acuity was reduced to an ability to count fingers (*Fig.* 225). The

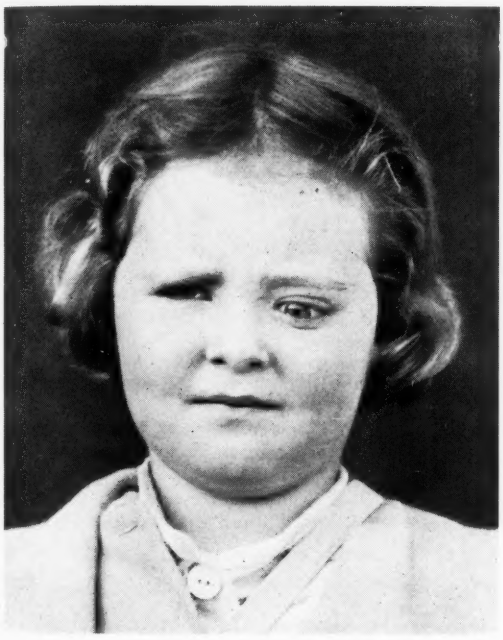

Fig. 225.—Photograph of patient before operation.

right eye was normal. There were no abnormalities demonstrable in the central nervous system, nor in any of the other systems.

A provisional diagnosis of intra-orbital neoplasm was made.

At Operation (May 1, 1946).—A right frontal osteoplastic flap was elevated, the frontal lobe retracted, and the orbital plate removed. On incision of the orbital fascia a swelling, covered with orbital fat, presented in the posterior part of the orbit. The muscle cone was not seen.

On breaking through the fatty covering of the swelling, a glistening cyst wall was revealed. Clear fluid was aspirated and the cyst wall was removed *in toto*. The bone-flap was replaced and the child recovered rapidly from operation. Examination of the cyst wall revealed typical laminated hydatid membrane (*Fig.* 226).

Following operation, the eye receded immediately to its normal position. Within a few days she developed marked œdema and ptosis of the upper eyelid and later a severe keratitis. There was also a paralysis of the superior rectus muscle.

On July 4 the eye was in normal position. The fundus was normal and external ocular movements were full. There was a small corneal scar.

For a time after operation the eye could be felt to pulsate, but this is now no longer evident.

COMMENT

Reference to literature (H. R. Dew's *Hydatid Disease*) indicates that hydatid cysts of the orbit are rare and, owing to the restricted space in which they develop, pressure symptoms appear early. The incidence is therefore more often upon young subjects. Trauma has been regarded as a causative factor, but this cannot be accepted, though it could lead to daughter-cyst formation. The cyst usually develops

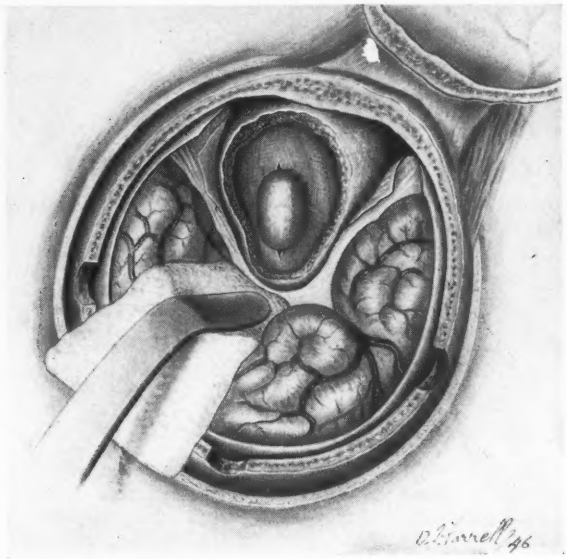

Fig. 226.—The cyst presenting on incision of orbital fat.

in the lateral or posterior region of the orbital cavity and causes gradually increasing pressure effects. Posterior pressure leads to papillœdema, retinal congestion, diminished visual acuity, and exophthalmos, whilst lateral pressure causes limitation of eye movements, strabismus, diplopia, and proptosis.

Pain, due to pressure on nerves or to secondary glaucoma, is occasionally the first symptom.

Particulars are given below of five reported cases (4 cases from Australia and 1 case from India).

Case 1.—Hardy, of Launceston, in 1879 reported the case of a female patient, aged 22 years, who had a history of pain and swelling in the left eye for three years. The eye was totally blind and proptosis was marked. The eye was removed and a cystic tumour was revealed, the contents of which were evacuated. Six months later the orbit was filled with a cystic tumour which was removed. No further report on the progress of this case was made.

Case 2.—H. M. O'Hara, in 1913, reported the case of a young woman of unstated age who complained of neuralgic pain in the eyeball and diplopia. Pain became intense and marked proptosis developed. Aspiration " between the eyeball and orbital plate " was performed and fluid withdrawn. The space was opened up (method

unstated) and the cyst removed. Recovery was uneventful, and there was immediate relief from pain and retraction of the eyeball to the normal position.

Case 3.—G. A. Pockley, in 1916, reported the case of a male aged 31 years who complained of failing vision, proptosis, and headache for three months. Eye movements were restricted and vision was reduced to distinguishing five fingers at 5 ft. The left disk was engorged and a radiograph was negative. Vision continued to fail and eye movements became absolutely restricted. The orbital cavity was exposed by Krönlein's method and a hydatid cyst removed from the nasal side of the optic nerve. Subsequently vision improved to 5/9.

Case 4.—M. Gardner, in 1924, recorded the case of a child aged 6 years who reported with proptosis over a period of three months. Proptosis was forwards only and papillœdema was present. V.A. 6/18. One month later, proptosis was in a downward and outward direction. A cyst was removed using Krönlein's method of exposure. After operation papillœdema subsided and V.A. was 6/6. On the day after operation the Casoni reaction was positive and there was a 15 per cent eosinophilia.

Case 5.—V. P. Patel, in January, 1933, reported the case of a 12-year-old Mohammedan boy in Karachi who had a swelling the size of a small orange of the right lower eyelid and cheek. The eyeball was displaced upwards and inwards. There was a history of a kick by a donkey six months previously, and the swelling had increased day by day since this event. The method of treatment and the outcome is not stated. The case is quoted to suggest that trauma plays a part in aetiology. The author does not state whether daughter cysts were present, though the cyst appears to be simple in the photograph illustrating the article.

Other cases in Australia have been reported by MacGillivray (1865), Gray (1880), Gasse (1883), and Burkitt (1908).

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ACUTE APPENDICITIS SIMULATING GALL-STONE ILEUS

BY G. E. MOLONEY

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THIS case is presented as an interesting example of a rare disguise for that great masquerader, acute appendicitis.

CASE REPORT

HISTORY.—J. S. (R.I. No. 65705/46), aged 50, a builder's labourer, was admitted to the Radcliffe Infirmary on Dec. 12, 1946. Forty-eight hours previously he had been seized with colicky pain in the epigastrium. The pain lessened after four to five hours, but did not disappear. His bowels had moved twice a few hours before the onset of the pain. On the next day the pain was easier and pulse and temperature were still normal. About ten hours before admission severe colicky pain returned but was now felt in the hypogastrium, and during the subsequent few hours he vomited three times. His doctor sent him to hospital as a case of intestinal obstruction. On admission his complaint was of constant pain across the hypogastrium. There had been no bowel action since the onset of his pain and the only flatus passed had been two small amounts in the last twenty-four hours. His urinary functions were normal. There was no history of previous abdominal pain, indigestion, or flatulence.

EXAMINATION.—The patient was a subdued, well-nourished, middle-aged man. The temperature was 99° F., the pulse-rate 100. His tongue was coated but not dry and his breath fœtid. The abdomen showed moderate distension and was tender at all areas below the umbilicus, with raised resistance at all areas. The percussion note was tympanitic; the bowel sounds were increased in frequency and had the quality associated with distended coils. The hernial orifices were normal. Rectal examination revealed a small amount of crumbly fæces and slight tenderness on moving the prostate, but above it I could not reach. The urine was normal.

Radiography.—Plain radiographs of the abdomen in sitting and supine positions were taken on the way to the ward (*Fig.* 227). These were seen and subsequently reported on by Drs. F. Kemp and K. Lumsden as follows: "There is evidence of distension of coils of small intestine with gas and fluid. There is also in the right lower quadrant of the abdomen a large opacity showing a laminated structure. Conclusion: The appearances are consistent with a low small-bowel obstruction. The opacity in the right lower abdomen may possibly be due

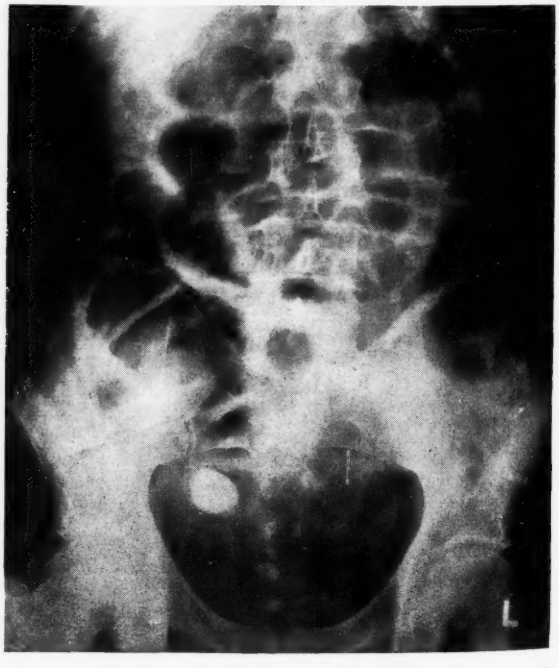

FIG. 227.—Supine radiograph showing distended coils of small intestine and the opacity in the pelvis due to the large fæcolith.

to an impacted gall-stone causing obstruction." I saw these films late at night and came to a similar conclusion.

After the administration of an enema, which produced a few small pellets of fæces only, and the passage of a stomach tube, which produced green-tinged clear contents in small amounts, the patient was taken to the theatre.

AT OPERATION.—Under pentothal and ether anæsthesia the abdomen was explored through a lower right paramedian incision. Distended loops of small bowel presented in the wound, moistened by a slightly turbid free fluid. A large gangrenous appendix containing a large fæcolith (*see Fig.* 228) was found lying over the pelvic brim, reaching to the midline, and adherent to overlying terminal ileum. Local paralytic ileus was evidently induced at the point of adherence, for the bowel above was dilated and that beyond was contracted. The appendix was gently separated and excised. The stump was treated by ligature and a double purse-string. Five grammes of sulphanilamide were dusted about the site of the lesion and the abdomen closed in layers with nylon sutures and no drainage.

PROGRESS.—For the next seven days the patient was in a state of paralytic ileus. He was given constant intravenous fluids and plasma, penicillin, and sodium sulphathiazole, and the Miller-Abbott tube was used for continuous suction. The tube eventually reached the cæcum, as shown by X-ray control. After seven anxious days return of bowel function was signified by the usual deluge of fluid fæces for twenty-four hours, after which normal bowel habits were established. There had been no sign of post-operative intra-abdominal abscess formation and no wound sepsis. He was putting on weight when discharged to a convalescent home on Dec. 28.

THE FÆCOLITH.—Size: $1\frac{3}{16} \times \frac{3}{4} \times \frac{3}{4}$ in. Composition: It consisted largely of organic material; the inorganic material present was calcium phosphate. Structure: It cut easily with a knife and there was a definite laminated appearance.

DISCUSSION

A large appendicular fæcolith is by no means rare, but to meet one of the size depicted here and to have its X-ray appearance in situ is most unusual. The chief point of interest, however, is in the diagnostic confusion to which it led. The shift of pain from epigastrium to hypogastrium with vomiting was consistent with a Murphy's sequence for pelvic appendicitis. But the presence of secondary intestinal obstruction, proved by radiological appearances, was sufficient to confuse the symptomatology with one of a moving gall-stone which finally impacted. The two radiologists and all the half dozen surgeons who have seen the radiographs diagnosed gall-stone ileus on radiological appearances. In conjunction with the clinical aspect of the case, the diagnosis appeared to be undoubtedly one of intestinal obstruction, as was in fact present; but the lack of a history suggestive in any way of antecedent abdominal trouble made one approach the "temple of mystery" with a tentative diagnosis of gall-stone ileus, but with a rider to the verdict that we were ready for instruction. As an afterthought, the only other diagnosis which might have been entertained, other than the real one, is that of a displaced enterolith producing obstruction.

The only other aspect of the case worthy of note was that the Miller-Abbott tube, which passed into the duodenum within twenty-four hours of swallowing, appeared to render undoubted comfort and much benefit, and was possibly life-saving.

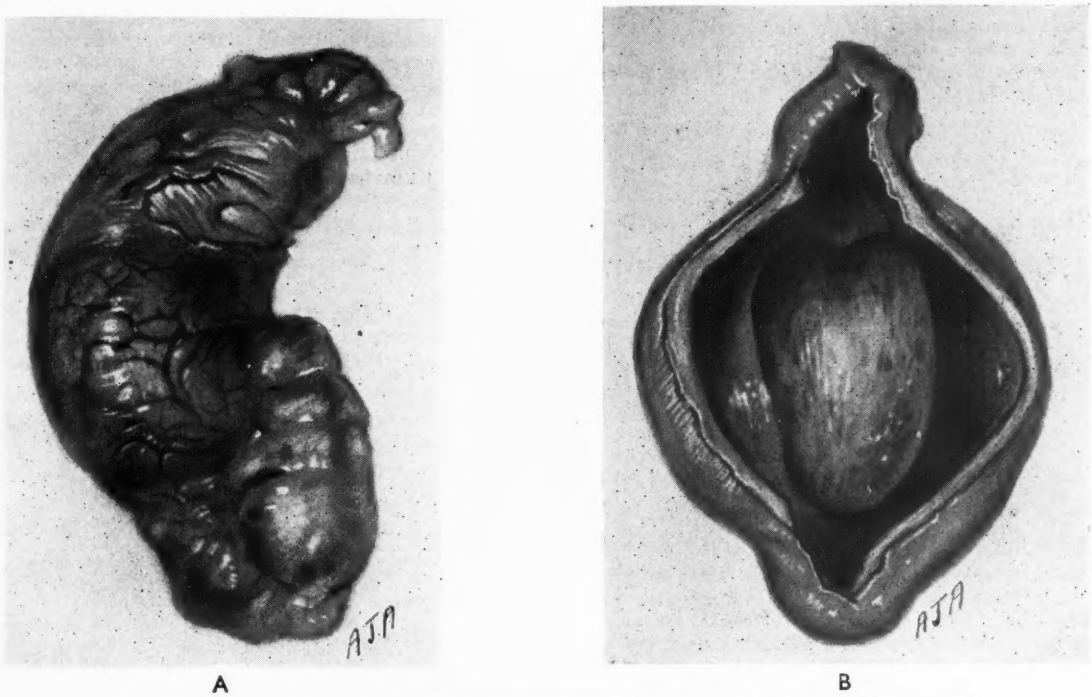

FIG. 228.—The appendix, before and after section, demonstrating the large fæcolith. (*Natural size.*)

I am indebted to Sir Hugh Cairns for helpful criticism, to Dr. F. Kemp for the radiograph, and to Miss A. J. Arnott for the illustrations of the appendix.

A GIANT ADENOSARCOMA OF THE BREAST

By HENRY DAVIES LLEWELLYN

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CASE REPORT

Mrs. M. A. Davies, a pensioner aged 78 years, was admitted to Llanelly General Hospital on Aug. 27, 1946, complaining of great enlargement of the left breast. She had been feeling unwell for the past twelve months, and had first noticed a small lump in the breast. The lump grew and the breast "felt very hard". She never had

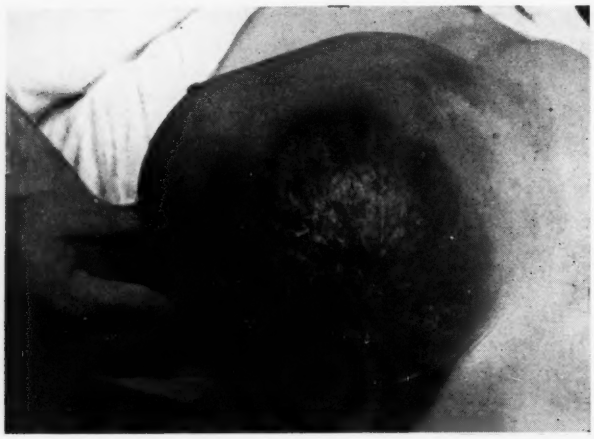

FIG. 229.—Showing the breast greatly enlarged by the tumour.

to stay in bed, and the breast only became painful a few weeks before her admission. She then had paroxysms of pain which were very severe and kept her awake at night. The tumour gradually increased in size over a period of twelve months.

ON ADMISSION.—The general condition was fair. The left breast was greatly enlarged, measuring 12 × 12 in., and appeared to be wholly occupied by a firm, smooth, well-defined tumour (*Fig.* 229). The mass was not attached to the underlying pectoral muscles or the

FIG. 230.—The tumour on removal.

nipple, but the overlying skin was adherent and discoloured by pressure over the more prominent parts of the tumour.

There were no palpable glands in either axilla or supraclavicular triangle, and the opposite breast was normal. The liver was not enlarged.

Radiographs of the chest, spine, humeri, and femora for metastases were negative.

In view of the abscence of evidence of local infiltration or metastases, a diagnosis of benign tumour was indicated, although the rapidity of growth suggested local malignancy.

OPERATION (Aug. 29).—Performed under pentothal, oxygen, and cyclopropane anæsthesia. A blood transfusion was given before and during the operation. A large, encapsulated tumour of the breast was removed intact, and found to weigh 11¼ lb. Convalescence was uneventful, and three weeks later the old lady was discharged.

PATHOLOGICAL REPORT.—The specimen consists of a large mass measuring 20 × 14 × 12 cm. surmounted by a generous ellipse of skin surrounding a nipple (*Fig.* 230). The tumour is well encapsulated. The cut section shows a dense whitish and pinkish tissue in which there are numerous blood cysts, 10–15 mm. in diameter, and areas of necrosis.

Histologically, five sections were examined (*Fig.* 231). They showed a mixed tumour of the breast, initially an intracanalicular fibro-adenoma in which the fibromatous

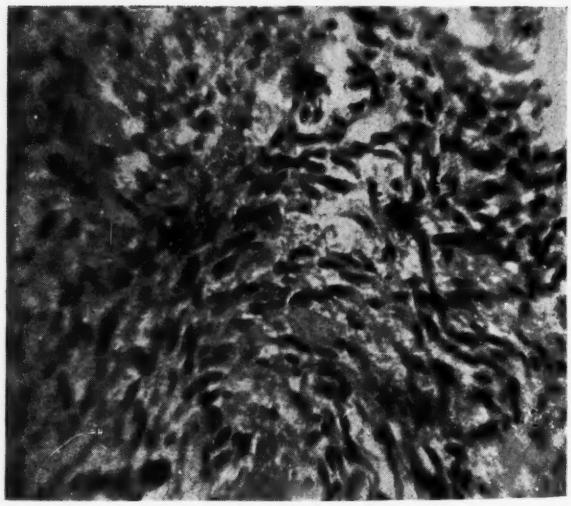

FIG. 231.—Microscopical section (*see text*).

tissue had hypertrophied to an unusual extent, appearing in some areas as a highly cellular fibroma and in others showing sarcomatous changes of low-grade type. There is much necrosis and cyst formations in the adenomatous areas of the tumour, but no evidence of neoplastic changes in the epithelial cells. The necrotic areas show inflammatory reaction in the surrounding tissue.

DISCUSSION

This case presents a number of interesting features. In spite of her advanced age, the old lady survived the ordeal of a major operation, and her comfort was greatly increased by the removal of so bulky and heavy a tumour. Operation had been witheld six months previously, when the tumour was considerably smaller, on the grounds of age, and the subsequent history emphasizes the point that age alone is no bar to procedures of this character.

Pathologically the tumour appears to have been an adenosarcoma. The development of sarcoma in

a fibro-adenoma is well established, but uncommon. The present specimen is chiefly remarkable for the large size attained by the tumour whilst remaining circumscribed. The specimen weighed 4650 g. This appears to be a record.

Prognosis as regards prolonged survival is fair. Geschickter found 11 cases of sarcoma secondary to fibro-adenoma in a series of mammary sarcomata. Of these 3 remained well and 8 died. Death was generally due to pulmonary metastases.

SUMMARY

1. A report is given of the successful removal of a giant adenosarcoma, weighing 4650 g., from a woman aged 78.

2. The value of such a procedure in the elderly is emphasized.

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HERNIATION OF THE URINARY BLADDER: 'DUMB-BELL BLADDER'

By FRANCIS E. STOCK

LECTURER IN SURGERY, UNIVERSITY OF LIVERPOOL

CASES of inguinal hernia in which the urinary bladder forms part of the contents comprise only a small fraction of all cases of hernia. Usually the herniation is small and can be reduced without difficulty. A case has recently been described (Bell et al. 1947) in which a large diverticulum of the bladder was found adjacent and adherent to the sac of a recurrent hernia. The occurrence of a combined direct and indirect hernia, the former irreducible and containing a major portion of the bladder, is therefore of interest.

Herniation of the bladder in association with inguinal hernia occurs in about 1·5 per cent of cases (Wakeley 1939), and in the same paper a description and classification of such cases is given.

CASE REPORT

Early in January, 1942, an adult male, aged 30 years, of the Yoruba tribe, was admitted to the African Hospital, Lagos, Nigeria, complaining of a swelling in the left groin. On examination he was found to have an inguinal hernia which was partially reducible, but a large irreducible mass remained at the neck of the scrotum. There were no symptoms or signs relating to any other disease.

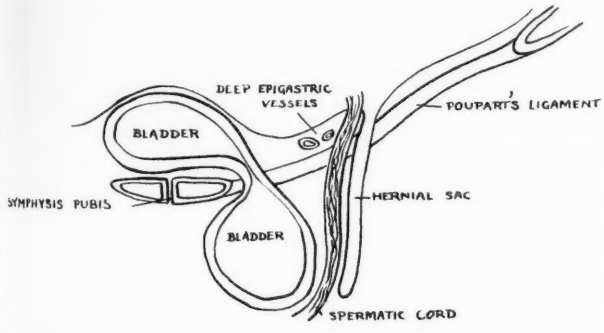

FIG. 232.—Diagram showing the dumb-bell shape of the bladder due to its herniation into the inguinal canal.

On Jan. 15 herniorrhaphy was performed under spinal stovaine. A small indirect hernial sac was identified, dissected off without much difficulty, and excised in the usual way. An attempt was then made to free the mass at the neck of the scrotum, which was seen to arise above the inguinal ligament. The mass was extremely adherent to surrounding structures, and in the course of dissection an opening was made into it and urine escaped. By means of a probe through the opening it was discovered that the extrapelvic mass was part of the bladder and was approximately equal in size to the bladder remaining within the pelvis, the whole bladder thus having a dumb-bell shape (*Fig.* 232). The mass in the inguinal canal was not a diverticulum in the ordinary sense for the wall consisted of all the coats of normal bladder wall. In view of the extreme constriction between the two portions of bladder, no attempt was made to reduce the swelling back into the pelvis, and partial cystectomy was decided upon. The projecting portion of the bladder was excised and the bladder repaired in layers by interrupted catgut sutures. The posterior wall of the inguinal canal was repaired by turning down a flap from the sheath of rectus abdominis. A catheter was inserted and tied in place.

The first and second post-operative days were uneventful. On the third day, however, the patient absconded from hospital during the night and nothing further was heard of him for fourteen days. On the seventeenth day after operation, he appeared in the out-patient department with the catheter still in place and the stitches still in. There had apparently been no leakage of urine from the wound. The catheter and stitches were removed. The urine was cloudy but not grossly infected. The patient left hospital and nothing further was heard of him.

Comment.—This case presents several interesting features: the extraordinary size of the vesical herniation, the limits to which early rising may be carried by an adventuresome patient, and the minimal urinary infection despite the long period of the indwelling catheter and absence of chemotherapy. The bladder hernia appears to fall into Wakeley's extraperitoneal group as it alone passed through the external abnominal ring, the small indirect sac being confined to the inguinal canal.

I wish to thank Miss B. Duckworth, artist to the Department of Surgery, The University of Liverpool, for the illustration.

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REPORT OF A CASE OF SPONTANEOUS PERFORATION OF THE ŒSOPHAGUS SUCCESSFULLY TREATED BY OPERATION

By N. R. BARRETT, London

Spontaneous perforation of the œsophagus has been discussed at length in a number of papers (Barrett, 1946; Foggitt, 1946; and Phillips, 1938) which have been published recently; the condition appears to be more common than has been supposed. The œsophagus may perforate either as a result of trauma, or as a result of some pathological process starting within its lumen, or the healthy œsophagus may rupture spontaneously during a paroxysm of violent vomiting or coughing.

In a review dealing with *spontaneous rupture of the œsophagus* published in 1946, I found that about 50 undoubted cases have been recorded in the literature, and amongst these no patient had survived the catastrophe. The concluding remarks in this paper were as follows: "In the byeways of surgery there can be few conditions more dramatic in their presentation and more terrible in their symptoms than spontaneous perforation of the œsophagus. No case has yet been treated successfully and diagnosis has only been achieved in a very few before death, and yet there is no fundamental reason why this unsatisfactory position should not be improved in the future. Several things are essential to success: firstly, a knowledge that the accident can and does occur; secondly, a knowledge of the symptomatology; and, thirdly, an early diagnosis. Given these, I am convinced that surgeons will be able to save some of these patients by combining the principles, already well established in the cases of abdominal perforations, with those relevant to thoracotomy."

Shortly after this had been written we had occasion to test the truth of this statement, for the patient whose case history is described below was admitted to the Thoracic Surgical Unit at Horton War Hospital.

CASE REPORT

History.—The patient was a woman, aged 46, who first attended King's College Hospital in 1942. At that time she was suffering from recurrent attacks of swelling of the face and neck, gastric pain, and intermittent diarrhœa. After a period of investigation she was diagnosed as suffering from angioneurotic œdema and a series of radiographs were taken from which a diagnosis of duodenal ulcer was made. In November, 1942, she was discharged from the hospital feeling well and without symptoms.

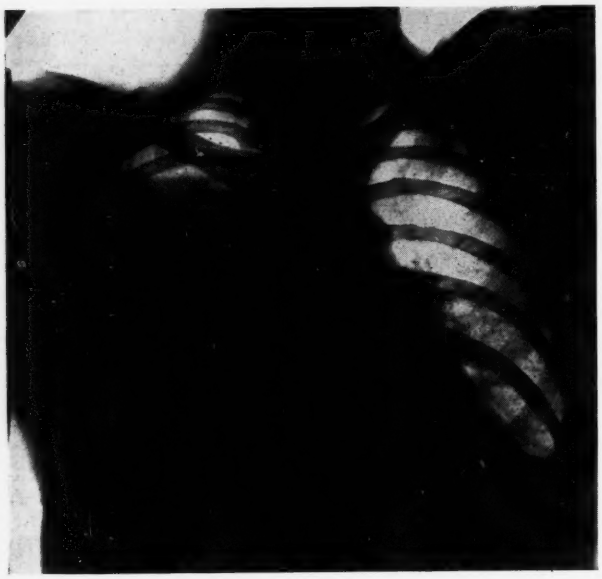

Fig. 233.—Radiograph taken a few hours after perforation of the œsophagus had occurred. The right pleural cavity contains a large amount of liquid and some gas.

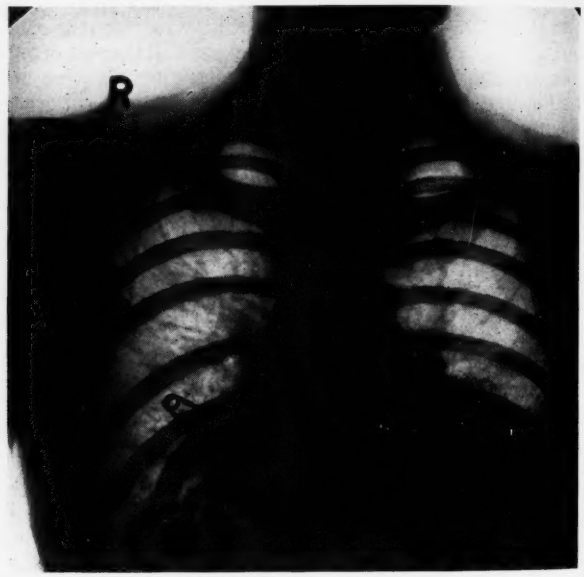

Fig. 234.—Radiograph taken on the day after thoracotomy had been performed. The right lung is completely expanded and the tube draining the right pleural cavity is functioning efficiently.

After this she suffered from repeated attacks of angioneurotic œdema and is also said to have had asthma. Her menstrual periods became very irregular and after a few months she became ill with the same symptoms and persistent attacks of dyspepsia. Clinical examination failed to show any evidence of sepsis. She was advised to take a light diet and was treated with intermittent injections of adrenaline. Radiographs of the stomach which were taken at this time showed no evidence of duodenal ulcer.

In January, 1944, she developed metrorrhagia and was admitted to Horton War Hospital under the care of Mr. Palmer. Lipiodol was injected into the Fallopian tubes and a dilatation and curettage was performed. This was followed by an attack of salpingitis. As her monthly periods had now become very irregular and her main symptom was profuse bleeding it was eventually decided to explore the pelvic viscera.

On Feb. 22, 1946, Mr. Palmer did a subtotal hysterectomy, a right salpingo-oöphorectomy, and a left salpingectomy, with partial oöphorectomy on the left side. The viscera in the pelvis were enlarged and adherent and there was much bleeding during the operation. Small tumours were palpable in the uterus and these were considered at the time to be adenomyomata.

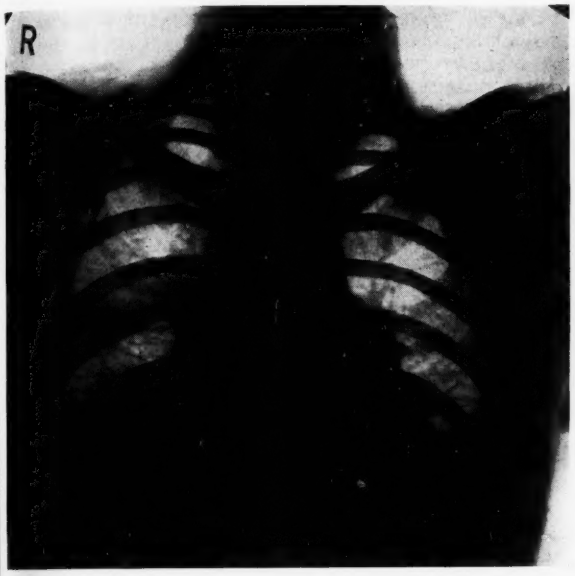

FIG. 235.—Radiograph showing the mediastinal abscess which developed during convalescence and which was treated by left-sided costo-transversectomy. The right pleural cavity was still being drained at this time.

The tissue removed at operation was reported upon as an endometrioma of the right and left cornua of the uterus, with long-standing chronic inflammation in the other parts.

After the operation her convalescence was satisfactory until the morning of March 7 when she was about to get up. She was sitting at the side of the bed at the time, when she felt sick and vomited violently. She immediately became cyanosed and dyspnœic and complained of agonizing pains at the back and lower part of the thorax, as well as in the epigastrium. The pain was accentuated by deep breathing. The upper abdomen was rigid and tender and the patient rapidly assumed the clinical picture of collapse. She was at first considered to be suffering from pulmonary embolism, but within four hours of the onset of the attack the percussion note at the right base was dull and there were physical signs indicative of a considerable amount of liquid in the right pleural cavity. Six hours after the onset of symptoms there was a slight improvement in her condition, but a radiograph of the chest (*Fig.* 233) showed a large collection of liquid and some gas in the right pleural cavity. An hour later her condition was critical. Her pulse was almost impalpable and she was cold, dyspnœic, and cyanosed. The whole of the right chest was now dull to percussion and two pints of liquid which looked like 'hospital tea' were aspirated. A rapid smear of this liquid showed it to contain pus cells and débris; an abundant growth of *Str. viridans* was ultimately reported from the laboratory. A diagnosis of spontaneous perforation of the œsophagus was made and operation was performed ten hours after the first symptoms had occurred.

OPERATION.—At the time of operation the patient was moribund and, apart from the signs in her chest, she presented the clinical picture of a perforated gastric or duodenal ulcer. A light general anæsthetic was given by Dr. Nosworthy and the right chest was opened by a long intercostal incision. About four pints of liquid gushed out from the pleura as soon as the cavity had been opened. This liquid looked like weak tea and contained small pieces of meat and other food. The pleura itself was not grossly abnormal and there was no fibrin on the surface of the lung. As soon as the tension had been relieved her condition improved enormously and a vertical slit about $\frac{3}{4}$ in. long was found in the mediastinal pleura immediately above the diaphragm. In this area the pleura was opaque, white, and thick, and when the hole had been enlarged a considerable space was found in the mediastinum, which contained fluid and débris. A small perforation was then found in the œsophagus. It was

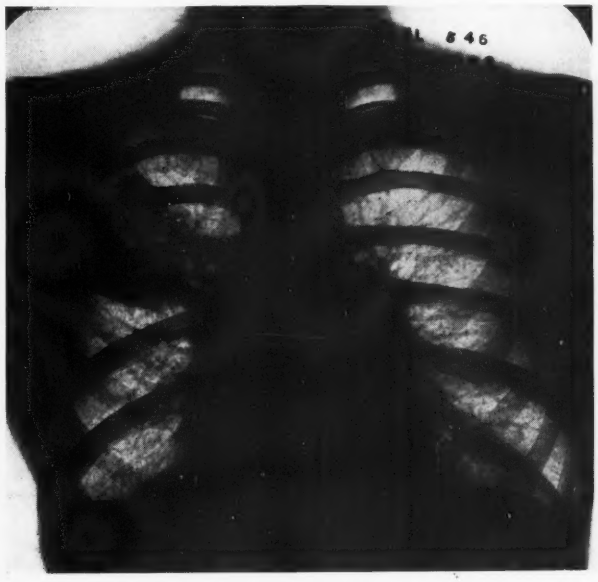

FIG. 236.—Radiograph showing that, although the patient has recovered completely from the mediastinal and pleural complications of the ruptured œsophagus, an acute abscess has developed in the right upper lobe of the lung.

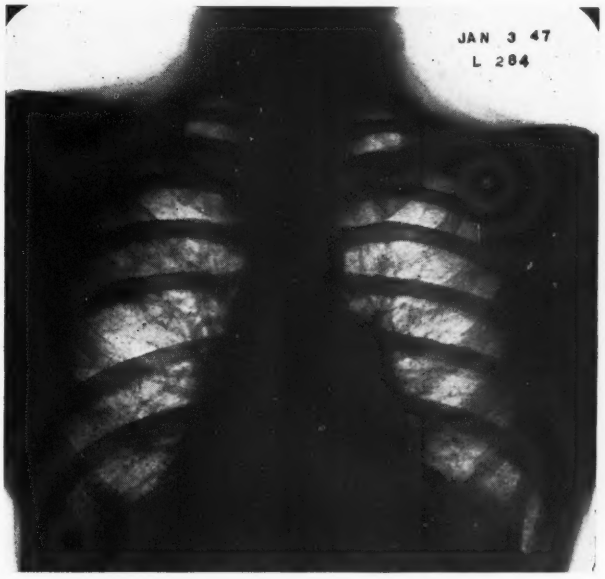

FIG. 237.—Radiograph taken 10 months after the first operation, at a time when the patient was clinically and radiologically normal.

situated about 1½ in. above the diaphragm and in the posterior wall of the viscus. The œsophagus was itself greyish in colour and had the appearance of chamois-leather. The perforation was closed with one purse-string suture of catgut. A drainage tube was inserted in the right pleural cavity and the incision in the chest wall was closed. During the operation the patient was given two pints of blood and at the end her condition was relatively good. The drainage tube was connected with a suction apparatus and she was put on a course of systemic penicillin of 20,000 units three-hourly. After the operation her condition rapidly improved. (*Fig.* 234.) A small amount of liquid was drained from the pleura but the œsophagus did not leak. She was put on a diet consisting mainly of liquids and given magnesium trisilicate by mouth. She was nursed in the sitting position.

PROGRESS.—Eight days after the operation she developed a sharp attack of asthma and on this day there was a small leak from the œsophagus. A Ryle's tube was passed and she was fed with a continuous drip of citrated milk. Her condition again improved and there was no further leak from the œsophagus into the right pleural cavity; but on March 26 radiographs showed a collection of liquid with a fluid level in the left side of the mediastinum and her condition again began to deteriorate (*Fig.* 235). This abscess was drained by a left costo-transversectomy and a fair-sized pocket was opened. At the same operation the abdominal cavity was opened and an enterostomy performed. Two days later her condition had again improved and after a short time it was possible to remove the enterostomy tube.

By May 21 she was completely convalescent and a barium swallow showed no definite abnormality of the œsophagus. There was no obstruction and no difficulty in swallowing. The right lung had expanded completely but a small patch of infiltration, which was thought to be tuberculosis, appeared in the right mid-zone (*Fig.* 236). During the next two months her condition remained excellent but, during this time, she developed an abscess in the right upper lobe of the lung which discharged spontaneously into the bronchus and which never caused her any serious illness.

Her condition in January, 1947, is satisfactory. She has no signs or symptoms referable to the lungs, œsophagus, or abdomen. (*Fig.* 237.)

This case is, I believe, the first in which spontaneous perforation of the œsophagus has been operated upon successfully.

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A CASE OF DERMOID ARISING FROM THE RECTAL WALL

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DERMOIDS in the wall of the rectum are rarely met with and the majority of cases reported so far have been of the nature of dermoid cysts. The following case is of interest in that the tumour was a solid fibromuscular mass with bony rudiments and had no cysts at all. It bore two rudimentary fingers.

CASE REPORT

The patient, a 17-year-old married Hindu woman, was admitted to King George's Hospital, Lucknow, with the complaint of a mass being extruded from the anus during defæcation for a duration of four months. She also complained of lower abdominal pain for about four years, which had become more marked for the last six months. Prior to the protrusion of the tumour from the anus the patient's attention was drawn to the fact that she sometimes passed hair in her stools and a few remained protruding from the anus after defæcation, which she pulled out herself. During an attack of typhoid several months before her admission she developed acute diarrhœa when she noticed long locks of hair in her stools. Whenever she took an aperient the passage of hair in the stools was very obvious.

ON EXAMINATION.—She was a well-built woman, physically fit. She had been married for two years but had no children. An oval mass 4 × 2 in. protruded out of the anal orifice on defæcation. It had two rudimentary fingers, one being longer than the other and had a well-formed nail. The longer finger measured 1¼ in. and was as thick as the little finger and the smaller one measured ¾ in. in length but was twice the thickness of the other finger. Long locks of hair were attached to the tumour which was easily reducible into the rectum.

On rectal examination the tumour was found attached to the mucous membrane of the anterior rectal wall by two pedicles ½ in. thick about 5 in. from the anal margin. The tumour was firm in consistence. Vaginal examination showed an acutely antiflexed uterus. The left ovary was palpable, but not the right one. The tumour was found high up and beyond the rectovaginal septum. There was no obvious connexion between the mass and any of the pelvic viscera other than the rectal wall.

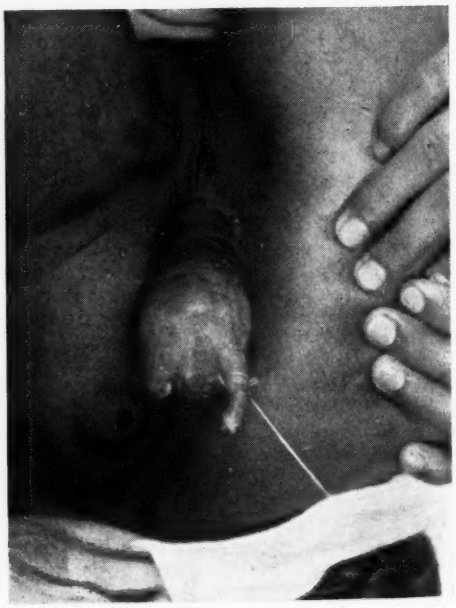

FIG. 238.—The dermoid extruded from the anus.

OPERATION.—The tumour was excised locally per rectum under general anæsthesia. Its attachment to the mucous membrane of the anterior rectal wall by the two pedicles was demonstrated and no intrapelvic connexion was found. The pedicles were divided with diathermy.

PROGRESS.—The patient had an uneventful recovery. Before she was discharged a radiograph of the abdomen was taken to exclude the presence of a similar tumour higher up the bowel.

THE SPECIMEN.—A description of the tumour has been given already and will be apparent from the photographs (*Figs.* 238, 239). It was a completely solid tumour. On section it was found to be composed of fibromuscular tissue. Each of the two rudimentary fingers contained a bony skeleton and there were several pieces of bone in the body of the tumour itself which were clearly brought out in the radiograph (*Fig.* 240). The largest piece was present at the base and measured 1 × 1 in. Long locks of hair were present around the base. There were no cysts and no teeth were found. It appeared to be a rudimentary hand attached to the anterior rectal wall.

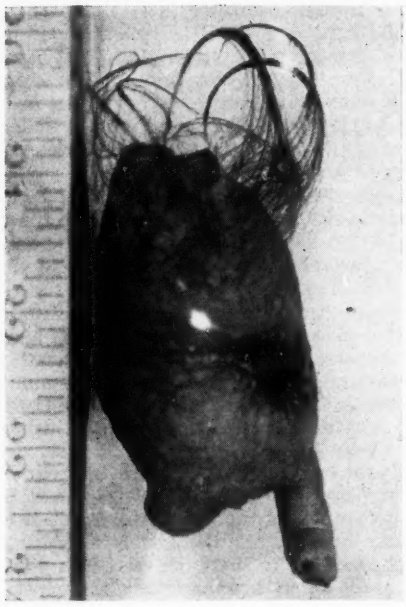

FIG. 239.—The tumour after removal.

FIG. 240.—Radiograph of the tumour.

DISCUSSION

Dermoids arising from the rectal wall have been occasionally reported in the literature. Bland-Sutton (1922), in his monograph on tumours, records several examples arising from the mucous membrane of the rectum. Gabriel (1937) refers to their rare occurrence. The commonest form in which they are met is as dermoid cysts, which are pedunculated and furnished with long locks of hair which protude from the anus and annoy the patient.

Soutter, quoted by Bland-Sutton (1922), describes cystic dermoids occurring in the rectum, of which two examples are preserved in the museum of St. Bartholomew's Hospital. One, removed from beneath the mucous membrane of the rectum of a woman aged 39, contained hair and teeth. The other, multilocular and as big as a fist, contained hair. This dermoid was detached and extruded during labour. A careful examination of the patient at the time of extrusion showed no communication with the pelvic cavity.

Nearly all the recorded examples of rectal teratomas have occured in women and this formerly gave some support to the suggestion that they arose in the ovary and eroded their way into the rectum. In a case reported by Moynihan, referred to by Bland-Sutton (1922), a teratoma was found between the layers of the mesocolon. The patient died in consequence of the operation performed for its removal. At autopsy the tumour was found in the connective tissue of the pelvis—the ovaries being free.

The idea that some of these teratoid growths were included fœtuses is a possibility. This could be reasonable when the tumour is situated around the terminal section of the gut, but it can scarcely be entertained when the tumour is high up in the rectal wall.

I wish to express my thanks to my father, Captain K. S. Nigam, Professor of Surgery, Medical College, Lucknow, for permission to publish this case, which was treated under his care.

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REVIEWS AND NOTICES OF BOOKS

The Results of Radium and X-ray Therapy in Malignant Disease. Being the Second Statistical Report from the Holt Radium Institute, Manchester. Years 1934–1938, inclusive, assessed at 5 years, and 1932 and 1933 assessed at 10 years. Compiled by RALSTON PATERSON, MARGARET TOD, and MARION RUSSELL. 1946. Edinburgh: E. & S. Livingstone Ltd. 7s. 6d. net.

THE first five-year Statistical Report was completed and published by the Christie Hospital and Holt Radium Institute of Manchester in 1939. It was an analysis of the work of the Institute for the years 1932-33, assessed at a five-year's interval.

In the first report the Chairman wrote a Foreword giving well-earned credit to the director, Dr. Ralston Paterson, and drew attention to the fact that the results of the treatment in malignant disease depend upon early diagnosis and immediate treatment. To this should be added what is obvious both in this and the second report—adequate follow-up by those skilled in the diagnosis and treatment of malignant disease in all its forms, and detection while still in an early stage.

In the preface to the second report Dr. Paterson is rightly proud of the fact that "except for twelve days in 1939 when war was declared, and the two days of the Manchester 'blitz' at Christmas, 1940, neither a treatment nor a follow-up clinic has been missed".

The report is a statistical survey of the work of the Institute for the five years since the first report, and of the ten-years' figures for the cases of 1932 and 1933. It shows what has happened to the patient on the fifth or tenth anniversary of treatment.

The report is from an "Institute of Radio-therapy", so the results are those obtained by radium or X rays, but occasionally combined with surgery for the primary growth. The Holt Institute, however, are firm supporters of surgery for removal of the secondary growths if there is the slightest suspicion of the glands being affected. Such surgical treatment, however, must be thorough and whenever possible a complete block dissection must be carried out, if necessary on both sides, should the growth be in the middle line.

The first report dealt mainly with radium therapy; during the interim period 'deep' X rays have been increasingly used. Both methods have their place and are often complementary.

The report is divided into three parts. The first deals with malignant disease as a whole, and, as the authors say, should interest everyone—layman, administrator, general practitioner, and specialist. To the doctor it will be a help for giving the friends and the patient, if necessary, a prognosis. Prognosis means literally to know beforehand—to do this with a modicum of success needs an immense experience, and even then the very elect may fail. It has been cynically said that the only thing of which we are sure is that we are not sure.

It is a science and art sadly neglected in medical education, though it interested Hippocrates. To prognose the outcome of a disease is often the first request of the friends and patient to the newly-qualified and practising doctor. A study of such a statistical report as this will be of material help.

The second part of the report is one in which is made "an attempt to evaluate different methods of treatment"—in other words, to give a prognosis.

The third part gives the ten-year results of cases treated in 1932 and 1933—again, then, prognosis.

Various sites are taken in considering the tables of results. The first is a consideration of all cases of malignant disease treated and then each region separately, e.g., skin, mouth, and lip, breast, uterine cervix and body, pharynx, larynx, maxillary antrum, rectum, and urinary bladder.

Cancer in these sites is easily approachable by radium or X rays. There are many other sites, however, in which cancer is common which at the time of the first report were frankly inaccessible; but as the result of research and intensive work on methods of technique, many of which emanated from the Holt Institute, the use of X rays is being extended. The discovery of atomic energy has probably placed weapons in the hands of radiotherapists to relieve suffering as well as giving mankind in general the most powerful weapon for the destruction of the race.

Both reports must be read and studied in order to assess properly the value of radiotherapy in the treatment of malignant disease. Good as they are, the one essential factor necessary is "early diagnosis and immediate treatment".

The Cancer Act of 1939, whereby cancer was made a statutory disease together with tuberculosis and venereal disease, was passed for this purpose. It made the local authority responsible for the treatment of cancer. This did not mean merely operative or radiotherapeutic treatment, but treatment from the beginning to the end of the disease. This was no new idea, it was the one for which the cancer department of the Middlesex Hospital was founded in 1791. It involves the whole question of the care of the chronic sick and aged. This Act has now been engulfed in the National Health Act, but the experience gained by the efforts to put the treatment of cancer on a regional basis should be of great value to the Regional Boards in their endeavour to arrange the hospital services of the country in a similar manner.

The general practitioner will always be the first line of defence for the community against malignant disease. He should have every facility placed at his disposal for early diagnosis by specialists, radiotherapists, and pathologists. The diagnosis being once made, immediate treatment should be ensured, and then a proper follow-up by those skilled in the detection of early recurrence. The interest and support of the general practitioner should be maintained throughout by not cutting him off from all contact with his patient until the disease is beyond treatment and then returning his patient to him with the hope that he may make the remaining time comfortable.

It is truly in this last stage that the general practitioner is of inestimable value to his patient, but he will be of much more value, and have a greater interest, if he has been kept informed of the progress of the case from the first, having seen the difficulties of making a correct early diagnosis, and the effect of treatment by whatever means, surgery, radiotherapy, or both. It is the family doctor, who, by his advice and help, can encourage the patient to submit to a diagnosis, and treatment, and above all to undergo more treatment if the first has been inadequate or resulted in failure.

The main causes for delay in the patient consulting a doctor with any disease, is ignorance, fear, gullibility, and false modesty. The main cause for failure in early diagnosis is what Dr. Johnson would describe as "Ignorance my dear Sir, sheer ignorance".

The general practitioner and family doctor is and must remain in the front line in combating what is becoming a scourge. Cancer is after cardiovascular disease the commonest cause of death, and there is no doubt that it can be cured in the early stages.

The public and the doctor must be educated in order that this ideal may be maintained. The criticism of many

will be that the only result of trying to educate the public will be to frighten them to death. This is not true if properly done; the whole idea is to frighten them to live.

Demonstrations of Physical Signs in Clinical Surgery. By HAMILTON BAILEY, F.R.C.S. (Eng.), F.I.C.S., Surgeon, Royal Northern Hospital. Tenth edition, revised. $8\frac{3}{4} \times 5\frac{5}{8}$ in. Pp. 375 + xii, with 573 illustrations, a number of which are in colour. 1946. Bristol: John Wright & Sons Ltd. 30s. net.

TEN editions, seven reprints, two foreign editions published, four more in other languages in preparation, and another being negotiated are sufficient evidence that a book is popular and supplies a real want for those for whom it is intended, namely, students commencing the study of clinical surgery. It will be treasured by them not merely in those formative years, but later during all their 'clinical' life. It would be instructive to know how many copies of the subsequent editions, after the first, have been purchased by those who realized when the book was first published that it was the sort they had been looking for.

The author in the Preface to this edition says of the book that it "makes me, a practising surgeon without an official teaching appointment, feel greatly honoured, but, at the same time, somewhat embarrassed". Why? The honour must truly be great, but the embarrassment quite unnecessary. An official teaching appointment would have brought him into contact with relatively few students even over twenty years, whereas in the British Empire and U.S.A. he must have taught literally thousands, and that not merely in an out-patient clinic or ward round, but during those reflective periods when the thoughtful student is going over the cases he has seen. The author, and the book as his teacher, is always available to remind him of the physical sign which he neither looked for nor perhaps knew about.

The wonderfully clear photograph of the case shows him how important this neglected sign really is in the correct diagnosis; so it is looked for, duly noted, and memorized the next time the chance offers.

The only advantage the author would gain by an official teaching position is that his personality would also be transmitted to the student, but even that is not wanting owing to the clear incisive style of the writing, the clearness and cogency of the illustrations, and the method of arrangement of the demonstrations.

The historical footnotes add enormously to the value of the book to the student, it whets the appetite of the curious, and makes him realize the tradition of medicine which he has inherited and should determine him not only to maintain, but to enhance, it.

Every student commencing his clinical surgery should possess this book. He has just finished three years of intensive study in laboratories, and attended many lectures and demonstrations. The latter have all been carefully rehearsed by technicians, and the demonstrator is almost certain that they will 'come off'. He has studied anatomy with a dissecting manual by his side and found structures with his scalpel and forceps.

Any abnormality which he met which aroused his curiosity has probably been brushed aside as of no importance by a busy demonstrator. He may have been taught anatomy as a feat of memory with little or no reference to function. He thinks all is well and his memory will see him through his course; never has he had any time to pause and ask the reason why?

Physiology is not so good, he finds that curious anomaly "Two schools of thought"—there may be more, but why worry too much! Which is the professor's school? That is the one which will be favoured in the examination. It usually has not entered his head that his teachers do not know everything about the subjects they profess.

He then enters clinical medicine and at once is lost. The details of physiology and anatomy with which he is cognizant do not seem to fit in. As a matter of fact he has been precipitated into a research laboratory with insufficient background. The author quotes Sir Henry Wade's remark, "The wards are the greatest of all research laboratories".

The student needs guidance as to his method of approach to each case, and this book supplies it. In Chapter I the author states what he calls the seven stages of a surgical case—if the diagnosis is still found wanting after traversing the first six, then the seventh stage may well be not exploratory laparotomy but "mere oblivion, sans teeth, sans eyes, sans taste, sans everything", except the post-mortem specimen.

There is no need to pass the book under review in detail after ten editions; there should be no errors of commission—some may find those of omission, but the size of the book must be kept within bounds in these times.

The format and illustrations reflect great credit on all who took part in its production and the publishers have the satisfaction of knowing it is worthy of their firm.

The Causation of Appendicitis. By A. RENDLE SHORT, M.D., B.S., B.Sc., F.R.C.S., Professor of Surgery, University of Bristol; Surgeon, Bristol Royal Infirmary. $7\frac{1}{4} \times 4\frac{7}{8}$ in. Pp. 79 + viii, with 4 charts. 1946. Bristol: John Wright & Sons Ltd. 10s. net.

THIS book commences with a quotation from an article by the author in 1920, in which he emphasized the fact that though appendicitis had become more common, especially in the decade 1895–1905, yet no settled conclusion had been reached with regard to its causation. He then suggested that the disease might be caused by the relatively small quantity of cellulose being consumed by the population and the increased amount of imported and preserved food in the modern dietary. He now advances more evidence in support of his thesis, collected from many papers published in the interim, and also quotes statistics of the frequency of appendicitis in many parts of the world. He compares these figures with the differences in the diet in these various places. He particularly acknowledges his indebtedness to the work of Professor Sir J. C. Drummond and A. Wilbraham on *The Englishman's Food* (1939).

It is difficult to assess the frequency of appendicitis in the past both from the paucity of authentic records and the fact that it was not until the classical description published in 1886 by Reginald H. Fritz in the *Transactions of the Association of American Physicians* that the disease was recognized as definitely originating in the appendix, and named appendicitis. He did not, however, as the author states, publish 100 cases of the disease successfully operated upon.

Bills of mortality were first kept and published in the time of Queen Elizabeth about 1581. The author has searched these bills for a period 1629–1660, but there is no mention of appendicitis. In all probability definite cases occured, but their identity is masked by such terms as surfet, colic, stoppage of the stomach, vomiting, inflammation of bowels, etc. The numbers of such cases producing death lend evidence to this surmise.

Jean Fernel (1508–1588) recorded a case with post-mortem findings under the title of "The Iliac Passion" in 1567.

Saracenus (1642) recorded a case of what must have been a peri-appendicular abscess, and the first operation for the relief of this condition is that recorded by Mestiver in France in 1759.

A similar case was also published in 1812 in England by Parkinson.

In 1834 James Copeland, in his book *The Dictionary of Practical Medciine* (vol. 1, p. 277), first distinguished between inflammation of the cæcum, appendix, and the surrounding tissues.

The author states that Hancock was the first to report the successful removal of the appendix in 1848.

The disease had been known under various names, e.g., the iliac passion, the iliac phlegmon, and iliac abscess. It was probably Dupuytren who first associated this inflammatory condition with the cæcum. He stimulated Husson and Dance to publish an article expressing his views in 1827 and incorporated them in his *Leçons orales de Clinicale Chirurgie* published in 1833.

In 1837 John Burne, Physician to the Westminster Hospital, drew attention to the difference between inflammation of the cæcum and the appendix, and followed it in 1839 with another paper emphasizing that the appendix was usually the origin of perityphlitis. He suggested that the disease would be better described by the term typho-enteritis. For the next fifty years the origin of inflammation and abscess in the right iliac fossa was argued and discussed in many papers. The term 'perityphlitis' survived, though various types were discriminated according to whether the inflammation or abscess was around the cæcum, between the iliac fascia and the bone, or an encysted abscess round the appendix. The term 'paratyphlitis' was suggested by Oppolzer (1858) and Ziegler in 1885 used the name 'typhlitis' to designate inflammation of the appendix.

After the publication of Fritz's paper in 1886 the name appendicitis was accepted and has remained.

The cause of the death of Kings and Royalty has always aroused morbid curiosity. There seems no doubt that the author is right when he says that King Stephen (1135–1154) died from the disease, and in support of this quotes the *Chronicles of Kings of England* by Sir Richard Baker (1568–1645), published in 1643. It was almost 880 years before another case occurred, which was fortunately cured by surgery but delayed the coronation of Edward VII. Louis XV of France (the Well Beloved) probably suffered from the disease while with his armies in Lorraine in 1744. It is recorded that he was seized with intense colic on the night of August 7th–8th. He had fever, headache, and vomited three times. The attack was described by Richelieu as "un embarras gastrique, suite d'une indigestion, et. . . d'une coup de soleil". The doctors in attendance gave the cause of the attack various names "fièvre maligne", "fièvre putride", etc.

He got worse in spite of enemata and purgatives which acted well. His life was despaired of, when suddenly on the ninth day a remarkable improvement set in and he slowly recovered.

In 1748 Madame de Pompadour (Antoinette Poisson) became his mistress. She was described by a contemorary "Elle sait tout enfin excepté la morale". Her only child developed what was undoubtedly acute gangrenous appendicitis in 1754 and died.

It was to Madame de Pompadour that we owe the porcelain factory which was removed from Vincennes to Sèvres in 1759.

The author quotes convincing statistics proving that starvation and privation diminishes the incidence of appendicitis. During the war years 1915–18 the incidence diminished, and remained so in Germany and Russia for some years after.

Those in the higher and more wealthy classes of the population are affected more commonly than the poor. For example at a public school for boys (500) there were 19 cases over a definite period, while at a children's home (350 boys and 600 girls) during the same period there were only 4 cases—and these all in girls, whereas males are usually affected more commonly than females.

It is fair to assume that in the former case the diet was much more liberal than in the latter, in which fresh meat was taken in small amounts and not more than once a week.

Why then does the disease appear to have been uncommon in the Tudor and Stuart period, in which we know, from the writings of Pepys and others, that the diet was more than generous and huge meals were eaten.

The author agrees that this is difficult to answer but in all probability cellulose was also taken in plenty. It was not then the fashion to have only white bread.

There are other difficult questions to answer. There are families in which many members have had the disease—moreover it is much more common in some countries than in others, being twice as common in U.S.A. as in England.

All authorities agree that it is a rare disease in negro communities, unless they have taken to 'western' diet. In Trinidad and Barbados, where the black outnumber the white population many times, it is more common in the latter.

Vegetarians do not appear to be very prone to the disease.

The highest incidence of the disease in relation to the population which the author can find is in the Falkland Islands. The population he states was 2432 in 1936. The diet consists there mainly of mutton and bread—fish, butter, vegetables, and poultry are very difficult to obtain.

It is very rare in the Eskimo. Their diet is usually raw flesh. The disease is rare in animals, yet apes in captivity develop it.

To quote the author: "Old England used to feed itself, modern England imports its food. About 1870 the method of milling was changed, the old flat grinding stones were replaced by rollers of metal or porcelain . . . It is remarkable that the rise of incidence of appendicitis coincides so closely with changes in the milling of bread and also with the immense increase of food imports."

This might be placed before the responsible minister as a further reason to keep agriculture as a No. 1 priority. There seems no doubt that the earth contains the means of our salvation, or, as the modern press expresses it, "The earth is the Bank of England".

The author then examines the various theories which have been put forward to explain the causation of appendicitis, none of which he concludes have fully justified themselves, though there is evidence which favours each. There is no doubt that there is a relationship between throat infections and appendicitis, whether as a primary cause or aggravating factor is open to discussion.

There is no evidence that the disease is in any way endemic, it is certainly not epidemic like enteritis may be, but actinomycosis is a recognized cause. Trauma plays no part in its causation though from time to time the possibility is argued in the Courts.

Then there is the foreign-body theory. Every surgeon of experience has met with foreign bodies in the appendix and the stercolith is very common, and credited with a definite train of clinical symptoms. The absence of cellulose in the diet, according to J. Spencer (*Brit. med. J.*, 1938, **1**, 227) enables liquid fæces to pass easily into the appendix, where the fluid is absorbed and a stercolith is formed.

Moreover, as the author states, it has been shown by Wangenstein and Bowers, that there is a sphincter control at the base of the appendix which can produce a virtual obstruction when non-organic narrowing exists. Injection of water into the lumen of the appendix will sustain a pressure of 60–80 mm. of water without leaking into the cæcum.

In 1920 the author advanced the lack of cellulose theory and finds nothing has so far been advanced to make him change his opinion. He truly says "There was a time when every disease, in which diet played a part, was thought to be due to something the patient had

taken . . . recently we have become aware of diseases not due to an excess but a deficiency . . .

"Is it possible for appendicitis to be a deficiency disease?"

He finishes with the evidence that the cellulose-containing foods have been replaced by others in the modern dietary, e.g., modern white bread, and further states in support of his thesis : —

1. The time criterion is correct; from 1895–1905 there was a big change in the diet.

2. Cellulose-containing foods persisted in country districts longer than in the towns. The incidence of appendicitis was at first more marked in urban than rural districts. Now-a-days town and country feed alike.

3. In institutions more simple and 'old fashioned' and cheaper food is still used and the incidence is less amongst the inmates than in the general population.

4. Animals (apes) develop appendicitis when in captivity. It is also a fact that experimentally rabbits fed on cellulose-free diet develop intestinal inflammation (Von Knieren, 1885).

5. During periods of privation the incidence of appendicitis diminishes, e.g., in Russia and Germany after the last war.

The whole book is provocative, even if not absolutely convincing. It remains to be seen if our country's present privations, even if unpleasant, are not, so far as regards appendicitis, a blessing in disguise.

The Pathology of Traumatic Injury. A General Review. By JAMES V. WILSON, M.D., M.R.C.P. (Lond.), Major, R.A.M.C. (T.). Pathologist to Harrogate and District Hospital and the Royal Bath Hospital, Harrogate. With a Foreword by PHILIP H. MITCHINER, C.B., C.B.E., T.D., M.D., M.S., F.R.C.S. D.Ch., K.H.S. $9\frac{5}{8} \times 6\frac{3}{4}$ in. Pp. 192 + xii, with 61 illustrations. 1946. Edinburgh: E. & S. Livingstone Ltd. 20s. net.

"THE way that most men deal with traditions, even those of their own country, is to accept them all without applying any critical test . . . so unlaborious to most people is the search for truth; so readily do they accept whatever comes to hand."—*Thucydides*, I, 20.

Thus did Thucydides expound his views of historians in general, but as one of his modern commentators remarks "he had never attended a secondary school or University or been trained in methods of research, but he had had a double education, theoretical and practical".

In the foreword Major-General Philip Mitchiner, A.M.S., writes: "The object of this monograph is to summarize the literature of the subject in the light of the author's personal work and war experience". "Major Wilson gained a wide experience of his subject during service with the R.A.M.C. in Malta and has made important contributions to the subject."

The reader of this book will realize that Major Wilson has satisfied what would evidently have been Thucydides' requirements for a good physiologist and pathologist, and moreover his education has been both theoretical and practical in the study of traumatic shock in its widest sense.

It is an endeavour to subject to a critical analysis the physiological and pathological basis of the signs and symptoms of that most real yet elusive clinical condition which is implied by the term 'shock'.

It is a book which every candidate for the primary fellowship examination of the Royal College of Surgeons should study, and though on paper limited to one clinical condition yet this embraces so many signs and symptoms resulting from disease in general, that a careful reading of it makes an excellent introduction to a rational explanation of many morbid conditions.

In the preface the author points out that the problem of shock is as old as recorded medical history, and he adds it is likely to remain a major medical topic as "it is difficult to see how speed and safety may ever be so joined as to control the incidence of injury".

The book is all the better for being compiled during war service, where references were difficult to obtain and consult.

The style and opinions are, so to speak, more pure, being formed away from contamination with the views of others—in other words, as he says, he has endeavoured "to mention progress and at the same time outline difficulties and problems awaiting urgent solution, to deal with essentials rather than give a mass of irrelevant facts".

What a help it would be to the hard-worked clinician if others would follow this advice. It may be that good will come out of the paper shortage after all!

The subject interests all clinicians, surgeons, and physicians alike, whatever the branch of medicine in which their interests lie. The latest publication which the reviewer has read on the subject is "The Cause of Post-operative Shock" (Hunter, A. R., *Lancet*, 1947, **2**, 162) by an anæsthetist! Why not? Clinical medicine is one great whole and cannot be divided into watertight so-called specialties.

If an anæsthetist is not interested in post-operative shock— who is? It is another reason why there should be one unifying authority such as a British Academy of Medicine established in one central headquarters as soon as possible.

The book is divided into two parts. The first deals with the general pathology of shock under the headings of the closely allied clinical conditions produced by trauma, burns, crush injury and traumatic anuria, fat embolism, blast injury, and wound infection. Some of these conditions might be said by some to produce the clinical condition of collapse rather than shock. Wherein lies the difference? The popular press journalist gets over the difficulty very satisfactorily when in his snappy description of the result of an injury he writes "The shock of the injury was so severe that the man immediately collapsed and died".

The second part refers to the clinical symptoms resulting from injury to specific anatomical regions, viz., the chest, blood-vessels, abdomen, central nervous system, and skeletal system. Many surgeons may quibble with the author over points of detail, but the broad principles of the results of these injuries are sound and moreover have been confirmed and studied in one of the most intense theatres of the war where first things had to come first and there was little room for vague theories and possibilities.

It is impossible to review the book in detail. It is itself essentially a review, and any attempt to criticize it would only result in a 'Review of Reviews'. This might satisfy some as a time-saving expedient, but they would be only those who seem, judging by modern bookstalls, to revel in digests of various kinds. It must surely be these to which the following refers :—

> Yet Ah! Why should they know their fate
> Since sorrow never comes too late
> And happiness too quickly flies
> Thought would destroy their paradise.
> No more: where ignorance is bliss
> 'Tis folly to be wise.

One can only advise every medical student to buy and read and keep the book. The publishers have done everything they can to make the book attractive, and the author has spared no pains in criticizing and directing the reader amidst the contending theories along lines of sound pathology and common sense, which after all is not so very common.

It should be in all hospital libraries, as it is the type of book for those wonderfully educative hours when hospital residents argue about the cases.

BOOK NOTICES

[*The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.*]

L'Infiltration stellaire. Technique, Indications, Résultats. By G. ARNULF, Nancy. With a Preface by Professor R. LERICHE. $8\frac{3}{4} \times 6\frac{1}{2}$ in. Pp. 234, with 25 illustrations. 1947. Paris: Masson et Cie. 400 fr.

Nouveau Précis de Pathologie chirurgicale. $8\frac{3}{8} \times 6\frac{1}{2}$ in. Vol. III, Pathologie de la Tête et du Cou. By M. ARNAUD, J.-P. CALVET, L. LEGER, P. PETIT, and V. VEAU. Pp. 589, with 308 illustrations. Vol. VI, Pathologie de l'Appareil urinaire et de l'Appareil génital masculin, Pathologie de l'Appareil génital féminin. By R. COUVELAIRE, J. PATEL, and P. PETIT. Pp. 967, with 369 illustrations. Paris: Masson et Cie. Vol. III, 900 fr.; Vol. VI, 1450 fr.

Tratamiento quirúrgico del Cancer de la Vejiga urinaria. By Professor S. GIL VERNET. Official Report of the Fifth Spanish-Portuguese Congress of Urology held in Madrid, June 17–22, 1946, $10\frac{3}{8} \times 7\frac{5}{8}$ in. 70 pp., with 44 illustrations. Barcelona. Reprinted from *Medicina Clinica*, 1946, **7**, No. 5.

Bone Dystrophies. By F. Y. KHOO, Department of Radiology, College of Medicine, National Central University, Chengtu. $10\frac{1}{4} \times 7\frac{1}{4}$ in. Pp. 169. 1945: Chengtu: Canadian Mission Press.

Hey Groves' Synopsis of Surgery. Edited by Sir CECIL P. G. WAKELEY, K.B.E., C.B., Senior Surgeon to King's College, London, etc. Thirteenth edition. $7\frac{3}{8} \times 4\frac{7}{8}$ in. Pp. 637 + viii, with 193 illustrations and 13 coloured plates. 1947. Bristol: John Wright & Sons. 25s. net.

Physical Treatment of Injuries of the Brain and Allied Nervous Disorders. By K. M. HERN, M.C.S.P., In charge of Physiotherapy Department, Military Hospital (Head Injuries), Oxford. With a Foreword by Air Vice-Marshal Sir CHARLES P. SYMONDS, K.B.E., C.B., D.M., F.R.C.P. $8\frac{3}{4} \times 6\frac{1}{4}$ in. Pp. 96 + viii, with 34 illustrations. 1947. London: Baillière, Tindall & Cox. 10s. 6d. net.

British Surgical Practice. General Editors: Sir ERNEST ROCK CARLING, F.R.C.S., F.R.C.P., Consulting Surgeon, Westminster Hospital, and J. PATERSON ROSS, M.S., F.R.C.S., Surgeon and Director of Surgical Clinical Unit, St. Bartholomew's Hospital; Professor of Surgery, University of London. In eight volumes. $8\frac{5}{8} \times 6\frac{5}{8}$ in. Volume I. Pp. 486 + xxxii, with 50-p. index. 228 illustrations. 1947. London: Butterworth & Co. Price per volume £3, Index £1.

Retropubic Urinary Surgery. By TERENCE MILLIN, M.A., M.Ch. (Dubl.), F.R.C.S., F.R.C.S.I., Surgeon, All Saint's Hospital for Genito-urinary Diseases; etc. $9\frac{5}{8} \times 6\frac{3}{4}$ in. Pp. 208 + vii, with 163 illustrations, some coloured. 1947. Edinburgh: E. & S. Livingstone. 25s. net.

Radical Surgery in Advanced Abdominal Cancer. By ALEXANDER BRUNSCHWIG, M.D., Professor of Surgery, University of Chicago. $9\frac{1}{2} \times 6\frac{3}{4}$ in. Pp. 324 + xii, with 118 illustrations. 1947. Chicago, Ill.: The University of Chicago Press. (London: Cambridge University Press.) 42s. net.

The Rehabilitation of the Injured. By JOHN H. C. COLSON, M.C.S.P., Rehabilitation Officer, Birmingham Accident Hospital and Rehabilitation Centre. With a Foreword by Sir Reginald Watson-Jones. Volume 2: Remedial Gymnastics. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. 556 + xii, with 439 illustrations. 1947. London: Cassell & Co. Ltd. 30s. net.

Inter-Allied Conferences on War Medicine 1942–1945. Convened by the Royal Society of Medicine. Edited by Major-General Sir HENRY LETHEBY TIDY, K.B.E., M.D., assisted by J. M. BROWNE KUTSCHBACH, M.B., B.Ch., D.P.H. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. 531. Illustrated. 1947. London: Staples Press Ltd. 50s. net.

Radium Dosage; The Manchester System. Compiled from articles by RALSTON PATERSON, F. W. SPIERS, S. K. STEPHENSON, H. M. PARKER, M. C. TOD, and W. J. MEREDITH. Edited by W. J. MEREDITH, M.Sc., F.Inst.P., Christie Hospital and Holt Radium Institute, Manchester. $9\frac{3}{4} \times 7\frac{1}{4}$ in. Pp. 124 + vii, with 38 illustrations and 4 plates and tables. 1947. Edinburgh: E. & S. Livingstone. 15s. net.

Endogeneous Endocrinotherapy including the Causal Cure of Cancer Compendium. By Dr. JULES SAMUELS, Specialist for Endogeneous Endocrinotherapy, Amsterdam. $9\frac{1}{2} \times 6\frac{3}{8}$ in. Pp. 541, with 30 plates. 1947. Amsterdam: Holdert & Co. Price not stated.

Reconstructive and Reparative Surgery. By HANS MAY, M.D., F.A.C.S., Assistant Professor of Surgery, Graduate School of Medicine, University of Pennsylvania; etc. With a Foreword by JAMES BARRETT BROWN, M.D., F.A.C.S. $10 \times 6\frac{3}{4}$ in. Pp. 964 + xxi, with 363 illustrations in text and section of illustrated cases. 1947. Philadelphia: F. A. Davis Co. $15.00.